SURGICAL PATHOLOGY

McFARLAND

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BY

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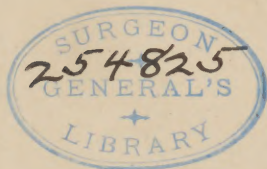THE UNIVERSITY OF PENNSYLVANIA

WITH 435 ILLUSTRATIONS

PHILADELPHIA
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1012 WALNUT STREET

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PREFACE

Surgical Pathology is not a separate subject, but merely the bringing together and emphasizing of those aspects of pathology that have been found to be of particular interest and importance to surgeons. Those beginning to specialize in surgery, frequently find themselves confronted by problems difficult to solve by recourse to the ordinary sources of information. It is for them that this book has been written.

Unhampered by convention and past precedent, the number of books upon the subject being small, the author was free to choose for himself what subjects he would consider, the order in which they should be arranged and the proportion of space assigned to each. Proceeding, therefore, along somewhat new lines, he presents not only accepted facts and theories, but lays before his reader, in concise form, the other theories that may have been suggested, weighing their relative values and criticising them.

The matter has been arranged in logical order and sequence, each part leading up to and explaining what follows. For example, much of the contents of Part I, which deals with "Congenital Conditions of Surgical Interest," is indispensible to an intelligent understanding of Part II that deals with "Tumors," as it contains all that is said about the Mixed Tumors, Branchiomas, etc., while the facts about the more simple Tumors being chief burden of Part II, scarcely anything need be said about tumors in Part III.

Two kinds of subjects have received particularly full consideration—those that experience has shown to be necessary to the student, and those concerning which the author has special knowledge. An overwhelming amount of his surgical consultations have had to do with morbid conditions of the Mammary Gland—which seems to be an organ much misunderstood and maltreated— hence particular attention and considerable space have been devoted to it.

A sincere attempt has been expended upon making the text interesting as well as profitable, and in order that its readability might not be diminished by repeated interruption, it has been broken as little as possible into chapters, sections and headed paragraphs.

In these days of frenzied activity, it is but rarely that a technical book is accorded the distinction of thorough reading. The stress of modern profess ional life is such that there seems to be but little time for that leisurely study that leads to scholarly attainment. Men rarely wander along the quiet paths of learning, but keep to the bustling highways, seeking for short cuts at high speed, as though their intellects like their bodies could be transported by automobile or aeroplane.

This book furnishes no short cut to knowledge or wisdom. It may be used as a book of reference, but it has been written to be read from cover to cover; for the breadth of knowledge to be thus gained as the student is led on step by step to the full understanding of the subject. It is not an encyclopedia, and

it should be understood that the mere reading of occasional scattered paragraphs will result in little benefit beyond refreshing the memory, and may defeat the very purpose of the writing by making any single part appear too brief or too inadequate.

The author is indebted to a number of friends for helpful suggestions given from time to time; for reading and criticising parts of the manuscript; for the loan of specimens and photographs, and for other kindnesses, and to them he again expresses his gratitude and tenders his sincere thanks.

A full index is supplied, as well as a bibliography in which most of the citations in the text, as well as a few useful ones not there mentioned, will be found.

<div align="right">JOSEPH McFARLAND.</div>

PHILADELPHIA.

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PART I

CONGENITAL CONDITIONS OF SURGICAL INTEREST

PART I

CONGENITAL CONDITIONS OF SURGICAL INTEREST

Occasional miscarriages of embryonal development result in anomalies and malformations, some of which are of surgical interest and importance.

Some show at the time of birth and leave no doubt as to their nature and origin; others not for years after, the connection then being obscured by the delay.

It is only through an intelligent understanding of the mechanism by which perfect development is brought about, that its anomalies and malformations can be fully understood.

The author's problem has been the selection and presentation of the important developmental aberrations without indulging in too extensive embryological detail.

Every omission may become a source of disappointment to someone seeking for information upon the matter omitted. It diminishes the usefulness of the writing as far as he is concerned, and at the same time subjects the author to the suspicion of having overlooked or been ignorant of the fact.

But between the covers of a single volume of practical size, the space neither permits the consideration of every subject, nor the complete discussion of any. The best that can be done is to treat each of certain selected subjects according to its merits in the limited space that can be assigned to it.

I. CONGENITAL MALFORMATIONS DEPENDING UPON CONDITIONS INHERENT IN THE EMBRYO, AND SHOWING A STRONG HEREDITARY INFLUENCE

A. DEPENDING UPON EXHAUSTION OR INHIBITION OF THE DEVELOPMENTAL FORCE—ARRESTED DEVELOPMENT

I. IN THE FACIAL REGION

Persistent Facial Fissures

About the second week of embryonal development, the large and prominent fore-brain vesicle at the anterior end of the embryo, bends sharply towards its ventral surface over the cardiac dilatation, and the visceral arches make their appearance. Between the fore-brain vesicle above, the cardiac dilatation below and the visceral arches at the sides there appears a deep depression, the "*oral pit*," which is the common beginning of the mouth, nose and pharynx. It is by the subsequent closing in and subdivision of this space that the face and its underlying cavities are formed during the fourth and fifth weeks of embryonal life, the whole being completed during the sixth week.

A prominent overhanging somewhat quadrilateral plate of tissue known as the "*naso-frontal process*" descends over the oral pit from the middle of the fore-brain vesicle, to form the greater part of the nose, its septum both cartilaginous and bony, its bridge, the vomer, the intermaxillary portion of the upper jaw, the soft parts of the nose, and the gutter in the middle of the upper lip sometimes called the *philtrum*.

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At each lower outer corner of the plate a considerable sized rounded mass, the "*globular process*" soon forms, and above each of these there is a distinct depression, the "*nasal pit*," about which the nostril is eventually formed. Above and to the outer side of each nasal pit is a bud of tissue, the "*internal nasal process*."

FIG. 1.—Early stage of the development of the human face in an embryo of about 29 days *np*, Nasal pit; *mxp*, maxillary process; *pg*, globular process; *os*, oral fossa. (*His.*)
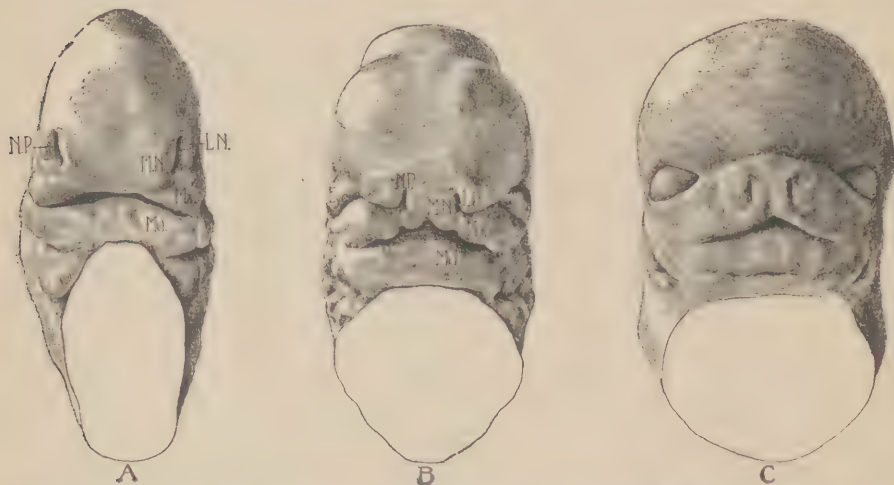
FIG. 2.—Development of the face in the second fetal month. *L.N.*, Lateral nasal process; *Md.*, mandibular process; *M.N.*, medial nasal process; *N.P.*, nasal pit; *Mx.*, maxillary process. (*From a series of models made in the Department of Embryology of the Carnegie Institution.*)

While these are forming, the uppermost of the visceral arches, the first or "maxillary arch" grows forward, dividing into two branches, an *upper* or *maxillary*, and a *lower* or *mandibular process*. The latter of these grows the faster, those from opposite sides soon meet in the middle line where they grow together, and thus the mandible or lower jaw is formed before the other details of the facial structure are far advanced.

As the various buds and processes grow and approach one another, they are found to be separated by certain regularly disposed intervals or fissures that

ever become narrower until they are obliterated by the final concrescence of the tissues. These fissures are quite as important as the processes they separate. If the latter fail to grow, the fissures remain open and malformation results. It is therefore necessary to consider the number and distribution of the fissures:

I. *The mandibular fissure* separates the two halves of the lower jaw. It is the first to be obliterated, and it very rarely remains open.

II. *The maxillary fissures* of which there are two, one on each side between the mandibular and maxillary processes of the first arch, which fuse to form the cheeks. If one or both fails to close, the size of the mouth remains excessive—*makroglossia.*

FIG. 3.—Patient with numerous facial fissures. (*Binney.*)

III. *The lateral nasal fissures* of which there again two, one on each side of the extreme lower portion of the naso-frontal process—that part that will eventually form the philtrum and the internal nasal process—and the lateral nasal process adjacent to it. Externally they appear to connect the mouth with the nostril of the corresponding side. Through their obliteration are formed the ridges that bound the philtrum on each side.

IV. The *oblique nasal fissures*, or as they are often called, the *orbito-nasal fissures*, one on each side, extend from the mouth to the orbit between the maxillary process of the first arch and the lateral nasal process of the naso-frontal process.

The growing buds by which the face is formed all tend to converge anteriorly towards the center, and the fissures by which they are separated to close from the lateral toward the median aspect.

By knowing the time at which the various concrescences take place it is possible to determine the age of the various facial malformations, but there is

very little of practical value connected with this knowledge as they all occur very early, the face being completed during the sixth week of embryonal life. The earlier the interruption of development takes place, the greater the resulting deformity will be. Thus, if it occur when the facial buds are but small eminences surrounding the oral pit, the result may be a monster without a face —a case of *schistoprosopia*—and in the front of whose head there is a gaping space. If it takes place later when all that remains is the closure, let us say, of one of the lateral nasal fissures, in order that the face be completed, there may remain the deformity known as a *hare-lip*, and according to the partial or complete closure of this fissure, the tissue separation may involve a narrow gap passing through the lip, the nose, the palate, and the superior maxilla almost to the orbit, or may show itself only by a superficial notch in the soft tissues of the upper lip.

The naso-frontal process and the maxillary branches of the first visceral arch, by which the entire upper part of the face is formed, not only form the face, but deeper structures as well. The former, not only forms the external and visible nose, but also the nasal bones that support it and vomer that divides it: the maxillary processes not only the upper parts of the cheeks, but the subjacent superior maxillary and malar bones, and through a shelf-like process the more distant palatal bone. It must not be conceived therefore that the developmental defects of these parts are limited to the soft parts or to the visible structures.

FIG. 4.—Median fissure of the face, which, not conforming to any of the embryonal fissures, probably resulted from the mechanical effects of amniotic bands. (*Le Dentu and Delbet.*)

A certain amount of confusion occasionally arises through the very rare occurrence of linear defects of the face, appearing as though referable to persistent facial fissures, yet having different anatomical distribution. For example, how shall a median fissure of the nose be explained? It is usual in these cases to hark back to the theory of Geoffrey Saint-Hillaire, who supposed that the facial fissures were caused by the pressure of amniotic bands. But a better explanation is the assumption that the naso-frontal process failed to grow down as it normally should, and left a gap that the other members were unable to close.

The observed malformations perfectly correspond to the theoretical possibilities, and comprise the following:

1. *Schistoprosopia*, a large central defect of the face caused by the failure of the numerous processes to develop. It is very rare, and is usually associated with fatal malformations of other organs.
2. *Agnathia*, or absence of the lower jaw. This results from arrested development of the mandibular processes of the first arch. It is not infrequently associated with synotia, or the meeting of the ears below the mouth. These cases are also rarely viable.

3. *Micrognathia* or abnormally small size of the lower jaw. It differs from the preceeding only in that there is a very small mandible instead of none at all. Synotia sometimes accompanies it.

4. *Makrostomia* or abnormally wide mouth opening results from unilateral or bilateral failure of concrescence of the maxillary fissures.

5. *Microstomia*, the reverse of the preceding, is the result of excessive concrescence of the maxillary fissures. It sometimes entirely closes the mouth —*atresia oris*—or there may be one or several very small mouth openings.

FIG. 5.—Makrostomia resulting from persistence of the maxillary fissure of the left side. (*Redrawn from Forgue.*)

FIG. 6.—Intermandibular fissure. (*From "Tumors, Innocent and Malignant," by Sir John Bland Sutton.*)

6. *Median Facial Fissure.*—This occurs in varying degrees. Thus there is first the vertical fissure of the nose to which reference has already been made with the suggestion that it arises through failure of the naso-frontal process to grow. Sometimes it seems to develop irregularly and lop-sidedly so that there may be one quite well formed nostril while on the opposite side there is a kind of snout. In other cases there may be no septum, and only one nasal opening which appears as a kind of proboscis. Occasionally both nostrils are well formed but separated by a median slit. In a case described by Bougon and Deroque there was associated fissure of the lip and palate.

7. *Oblique Facial Fissure.*—This results from failure of concrescence of the lateral nasal and maxillary processes and may be unilateral or bilateral. In some cases the former grows more rapidly than the latter of the processes mentioned, and a displacement follows, making the fissure assume a position justifying the appellation "vertical buccal fissure" which it sometimes receives.

8. *Lateral nasal fissure* results from failure of concrescence of the internal nasal bud of the naso-frontal process and the lateral nasal process of the maxillary process. It may be unilateral or bilateral, and is characterized by a linear defect of the upper lip along one edge of the philtrum, extending into the suprajacent osseous tissues by way of the nostril. It is the most frequent of all the facial defects and is known as "hare-lip."

Hare-lip

Hare-lip, Os leporinum, Bec-de-lièvre, or Hasenscharte, is a congenital defect caused by the failure of the lateral nasal fissure to close.

It may be limited to the soft parts or extend deeply into the osseous tissues, thus giving rise to at least three distinct forms:

Cheiloschisis, in which the lip only is affected,

Cheilognathoschisis, in which the defect in the lip is continued between the bones of the upper jaw, and

Cheilognathouranoschisis, or hare-lip complicated with cleft palate, in which the fissure continues through the jaw and palate so as to connect the nasal and oral cavities.

Any of these defects may be unilateral or bilateral. In the latter case the lesions of the two sides may be similar and symmetrical or may differ in depth and extent. An excellent classification of the subject by Delbet and Le Dentu, is as follows.

1. **Unilateral.**
   A. Simple.
   B. Complicated by a bony fissure.
      1st degree: With scarcely any noticeable cleft in the alveolar process.
      2nd degree: The anterior border of the maxillary bone is alone divided; a bridge of mucous membrane without bone passing almost to the anterior palatine foramen, the two edges masked by their muco-periosteal covering. The intermaxillary bone projects more or less markedly before the superior maxillary, and twists upon itself in such manner that the internal border of the breach is lifted up in front and behind. When any teeth are present, they are displaced in correspondence with the twist of the intermaxillary bone upon its anterior axis.
      3rd degree: The entire alveolar process is divided as well as the anterior part of the palatine arch. This portion of the breach has an oblique direction from above downward to the anterior palatine foramen where it stops.
      4th degree: This consists of a combination of the alveolo-palatine fissure with a velo-palatine fissure, of which it is a prolongation.
2. **Bilateral.**
   A. Simple. This deformity consists of a simple fissure of the soft parts on both sides. Though symmetrical so far as bilateralism is concerned, there may not be symmetry in the extent of the lesions. One side may show a little notch, the other a gap that reaches into the nares.
   B. Complicated. The osseous complications have several different aspects:
      (*a*) Alveolar fissure on the two sides with slight prominence of the intermaxillary bone.
      (*b*) Deeper fissure with preservation of the buccal mucosa that bridges over the gap.
      (*c*) Complete fissure involving the mucosa as well as the bony substance, and abutting by two converging lines from before backward to the anterior palatine foramen. In such cases it is almost the rule that the vault of the palate be divided. However, Lannelongue has reported a case in which it was intact. The forward projection of the intermaxillary bone increases in proportion to the depth of the fissures and the median labial lobe diminishes more and more. In these cases absolute symmetry is not the rule. On one side there may be a simple alveolar fissure, on the other a complete one, but such a combination is exceptional.
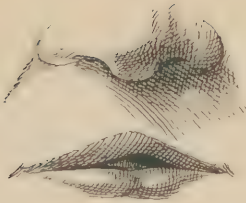
FIG. 7.—The most simple type of hare-lip consisting of a notch-like shortening near the center, but always toward one or the other side.

FIG. 8.—A more distinct variety consisting of complete division of the lip along one philtral junction.

FIG. 9.—A still more distinct variety in which the fissure in the lip is complicated by a fissure of the bony tissue extending into the nostril.
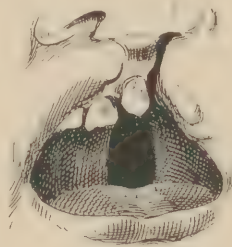
FIG. 10.—Complete division of the lip with a fissure extending into the nostril and complicated by a cleft in the palate.
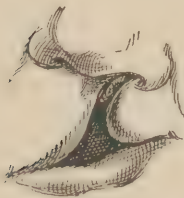
FIG. 11.—Left unilateral hare-lip with atrophy of the external part of the divided lip.

FIG. 12.—Left unilateral hare-lip with hypoplasia of the labial tissues.

FIG. 13.—Double hare-lip complicated by projection of the endognathion.
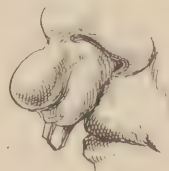
FIG. 14.—The same viewed from the side and showing the projection more distinctly.

The palatine fissures never exist alone, at least no such cases have been recorded.
Fissures of the palate always coexist with fissures of the velum. Those appearing
to be purely palatine are usually found to be continuations of breaches in the con-
tinuity of the maxillaries.

A. Simple cleft palate.
These are unaccompanied by hare-lip. They may be limited to the uvula, but
ordinarily the velum is split more or less, and it is rare for the bone not to partici-
pate to the length of one centimeter.

B. Complicated cleft palate.
In these the palatine fissure is associated with hare-lip.

That all of the malformations under consideration are the result of arrested
development is clear. The various fissures should have become obliterated
through the concrescence of the adjacent structures. Why did this fail? The
true explanation of the conditions is not to be found in the mere statement of
what has happened. There must have been some reason for it. At the very
beginning of the chapter it will be found that they are classified as depending
upon exhaustion or inhibition of the developmental force, a conclusion drawn
from the frequency with which the conditions are inherited.

Geoffroy Saint-Hillaire, the father of teratology, thought that the fissures
were the result of the presence of amniotic bands. That seems to be improb-
able, and Le Dentu points out that if so, their anatomical distribution would
scarcely conform so perfectly to that of the fissures, that some remnants of the
bands ought to be occasionally found, and that the persistent fissures ought to
be associated with other deformities also referable to the bands. To this might
be added the improbability of the occurrence of such amniotic bands throughout
families.

Hayman studied 47 families in which there was frequent occurrence of
hare-lip among brothers and sisters. He also studied 1857 cases for evidences of
inheritance, and found it is 8%. Later he more carefully studied 244 cases,
and found inheritance in 24% of them. Hauf, in Brun's clinic, examined the
personal histories of 555 cases and discovered either direct or collateral inherit-
ance in 11.35%. Le Dentu combining various published statistics came to the
conclusion that inheritance played a part in the occurrence of the deformity in
16.5%.

The hereditary influence may be derived either from the paternal or maternal
lines. In Hayman's cases, paternal influence was observed in 30, maternal in 25.
He thought that the occurrence of the malformation tended to become more
frequent as it was passed down from generation to generation. Schmitz
observed that it occasionally skipped one or more generations. Le Dentu
found that it occurred more frequently where consanguineous marriages were
practiced.

It seems quite certain that where there is such marked hereditary influence,
the condition cannot be accidental, but must find explanation in some disturb-
ance of the germplasm itself. There seems to be no better term by which to
describe the fault than that used, "exhaustion of the developmental force."

But what is the matter with the developmental force? Why is it thus
exhausted? It is not a matter peculiar to hare-lip and cleft palate, but as will

later be seen, one that applies to many malformations of many different parts of the human anatomy. Many have wrestled with the problem with little success. In the conclusions one is apt to see reflected the thoughts paramount in the minds of the writers. This is well indicated in the opinion of Fournier. Being a syphilographer, and knowing the destructive tendencies of that disease, he considers all of these congenital disturbances as resulting from an exhaustion of the developmental force due to syphilis in one of the antecedents by whose disease the stock was rendered defective and its vegetative forces weakened.

Another might equally see the weakening of the vegetative and vital forces resulting from tuberculosis or some other constitutional malady. There is no conclusion possible. Somehow, in some case, the defect occurs, after which it tends to perpetuate itself through the disturbance of the germ-plasm.

Haug's examination of the 555 cases from Brun's clinic, showed the following relative frequency of the different varieties of hare-lip.

Unilateral simple hare-lip.. 130 cases
Bilateral simple hare-lip... 18 cases
Unilateral labio-maxillary fissure............................... 21 cases
Bilateral labio-maxillary fissure, with one or two fissures in the
    alveolar process... 6 cases
Unilateral labio-palatine fissure................................ 27 cases
Bilateral labio-palatine fissure................................. 12 cases
Unilateral labio-maxillo-palatine fissure........................ 226 cases
Bilateral labio-maxillo-palatine fissure......................... 83 cases
Unilateral hare-lip with unilateral labio-maxillo-palatine fissure..... 32 cases

Various authors have studied cases with reference to the sex of the patient:

AUTHOR	CASES	MALE	PER CENT	FEMALE	PER CENT
Bein.....	708	441	62	267	38
Fahrenbach...................	210	143	68	67	32
Haug........................	463	287	63	176	37
	1381	871	64	510	36

The same authors also tabulated the cases with reference to unilateral and bilateral occurrence as follows:

AUTHOR	CASES	UNILATERAL	PER CENT	BILATERAL	PER CENT
Bein........................	708	552	72	187	27
Fahrenbach..................	210	152	74	58	26
Haug.......................	555	420	76	135	24
	1473	1124	73	380	26

Also with reference to the side affected as follows:

AUTHOR	CASES	LEFT	PER CENT	RIGHT	PER CENT
Bein........................	523	372	71	187	27
Fahrenbach..................	152	112	74	58	26
Haug.......................	420	291	69	129	31
	1095	775	71	338	28.6

When a hare-lip involves the soft tissues only it is called *simple;* when it is accompanied by osseous fissure, *complicated.* The proportional occurrence of these is shown by another tabulation from Haug.

Simple unilateral hare-lip.................................. 130 cases—25%
Simple bilateral hare-lip................................... 18 cases— 3%
Complicated unilateral hare-lip............................ 247 cases—49%
Complicated bilateral hare-lip............................. 133 cases—23%

In cases of hare-lip complicated with fissures extending through the alveolar and palatal processes of the superior maxillary bones it is often an interesting matter to determine exactly where the fissures are. An examination of a number of cases leads to the conclusion that they are not always in exactly the same place, though at first it would seem that they ought to be. The explanation of this seeming discrepancy is to be found in the composition of the superior maxillary bone, which in the particular region interesting us at the present time is composited of three distinct portions. The innermost is called the *endognathion*, the next the *mesognathion*, and the outer the *exognathion*. In cases of complicated hare-lip with intermaxillary bones, the endognathion and mesognathion play an important rôle. It is known that they arise from separate

Internal intermaxillary or endognathion.

External intermaxillary or mesognathion.

Superior maxillary or exognathion.

Showing the open fissure between the endognathion and mesognathion of each side, the fissures most frequently concerned in hair-lip and the usual composition of the intermaxillary bone.
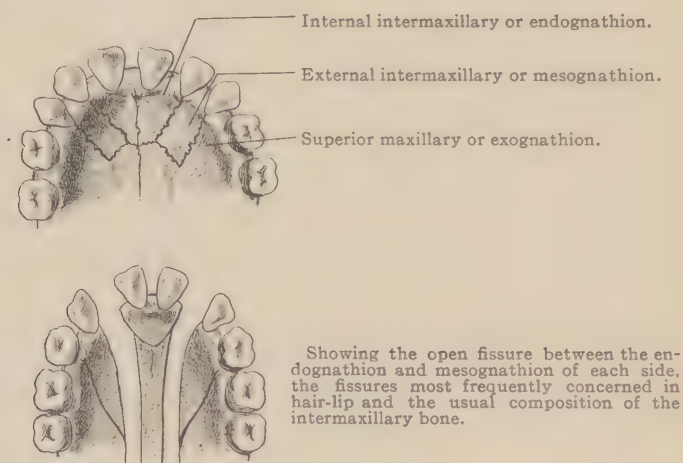
FIG. 15. —Diagram showing the different intermaxillary bones, and their relation to the teeth, in a child. (*Albrecht.*)

centers of ossification from those of other portions of the superior maxillary, but to what extent is uncertain.

In 1786 the German poet Goethe, who was also a scientist, interested himself in hare-lip and made an elaborate study of the bones concerned, arriving at the conclusion that the "intermaxillary bone is composed of two parts each of which bears two incisor teeth, and that the labio-alveolar fissure always passes between the lateral incisor and the canine teeth."

Later Coste took the matter up from the embryological rather than from the anatomical point of view adopted by Goethe, and came to the conclusion that the intermaxillary bones are formed in the internal nasal buds, and that hare-lip

results from failure of the internal bud to coalesce with the maxillary bud, thus placing the fissure where Goethe had found it. In 1879 Albrecht again took up the question, and opposed this view because he thought the external nasal process did not stop at the ala of the nose, but continued to grow downward to participate in the formation of the alveolar process between the internal process and the maxillary process, thus forming the external intermaxillary bone or mesognathion. According to this view there must be four intermaxillary bones, an external, the mesognathion, and an internal, the endognathion, on each side. He believed the fissure in hare-lip to pass between the endognathion and the mesognathion, the fault lying between the internal and external buds.

Kölliker and His, than whom there are no better embryologists, disagree with Albrecht, not finding that the external process descends as he says, but that it simply forms the wing of the nose and the walls of the nasal fossa.

It might be supposed that the position of the fissure with relation to the teeth ought easily to settle the question, but their imperfection and the irregularity of the bones in hare-lip, makes this impossible.

It really seems, however, that the fissure usually passes between the endognathion and the mesognathion. Broca found it there in 72 out of 100 cases, and Kirmisson in 14 out of 20 cases.

But the matter is not finally settled as far as the anatomists are concerned.

In cases of unilateral hare-lip there is little of interest or of practical importance connected with the exact position of the fissure, and the question seems like an academic one; but in cases of double deformity, the position of the fissure becomes a matter of great importance because the intermaxillary bones then fill the space between the fissures and project in an awkward and unsightly manner, sometimes projecting as a kind of snout and interfering with the correction of the deformity. A generation ago the surgeon operating upon such a case was wont to remove this bony tissue, but in doing so sacrificed the incisor teeth of his patient—two of them if the fissures passed between the endognathion and mesognathion, all of them if they passed between the mesognathion and the exognathion.

Some surgeons of more recent date have recommended preserving the bone by turning it back. In so doing, however, it is very important to remember that the germs of the incisor teeth are contained in the bony structure, which must not be so placed as to cause their eruption in a horizontal and useless position. The chief consideration in all these cases should be the proper preservation and disposition of the intermaxillary bone in order that the incisor teeth may be preserved and made subsequently useful.

In the coaptation of the tissues of the lips in the repair of hare-lip it is necessary to remove their dermal covering; in coaptating the bones in the repair of complicated hare-lip, it is similarly necessary to scratch away the delicate covering of ectodermal tissue by which the contiguous surfaces are kept apart.

Cleft Palate—Uranoschisis

At the same time that the face is forming and the features differentiating externally, the nasal and oral cavities are differentiating internally. From

the inner surface of each maxillary process of the first visceral arch, a fold of tissue, in the form of a kind of shelf, extends laterally towards the middle line, where it eventually meets its fellow of the opposite side and fuses with it. Thus is formed the palate, by which the nasal and oral cavities are separated. But the concrescence can miscarry at any point of development, and thus arise the different varieties of "cleft palate," or as it is technically called, *uranoschisis*.

FIG. 16.—Different varieties of cleft palate.   *A*, Fissure in the soft palate only; *B*, fissure of soft and hard palates; *C*, fissure extending through the alveolar borders on both sides and complicating hare-lip.   (*Redrawn from Forgue.*)

Circumstances interfering with the closure of the median and lateral nasal fissures on the outside, may also interfere with the closure of the fissures on the inside, hence the frequent association of hare-lip and cleft palate.

But the failure of the closure of the fissure between the lateral halves of the palate-forming structures, may occur independently of the others, hence the frequent independence of cleft palate.

The concrescence of the palatal tissues takes place from the front backward, and the arrest of development may occur at any point short of perfection. Thus, progressing from the most mild to the most exaggerated conditions, we find the following:

    1. Bifid uvula.

    2. Staphyloschisis—fissure limited to the soft tissues.

    3. Uranoschisis—fissure extending into the bony tissue of the palate.   In ordinary cases the defect in the bone is but the forward extension of the fissure in the soft structures.   It is only in very rare cases that the soft tissues are found joined behind a fissure in the bone.

There is usually a single cleft, but in cases complicating double hare-lip there may be two.   In unilateral unaroschisis the vomer is attached at the side opposite the fissure; in double uranoschisis it may hang in a central position and be unattached.

The obliteration of the facial and other fissures through the concrescence of the approximating tissues is sometimes attended by interesting complications resulting from the accidental inclusion of some of the embryonal material. Thus arise interesting recesses, cysts and tumors that will be considered under

a later caption, conditions depending upon the accidental dislocation of tissue during embryonal development.

Of these, one, the *inferior labial fistula,* is difficult to explain upon embryological grounds, though undoubtedly a defect of development, as it is both congenital and hereditary. It consists of a short sinus or blind fistula on one or both sides of the median line of the lower lip descends to a varying depth—usually but a fraction of an inch, and is lined throughout with stratified squamous epithelium. In his book, "Tumors, Innocent and Malignant," Sir John Bland-Sutton shows a family portrait of a mother, son and daughter, each with two symmetrical fistulae of this character.

FIG. 17.—Two symmetrical blind fistulae in the lower lip, having a depth of $3/4$ inch, with large mucous glands at the bottom. (*Brophy.*)

II. IN THE CERVICAL REGION

Differences of opinion in regard to the embryological development of the neck are the starting point of certain controversies regarding the origin of its anatomico-pathological defects.

In describing the development of the face it was pointed out that its lower portion was largely formed of substance derived from the first of five visceral arches, which make their first appearance during the second week of embryonal life, as buds along the ventro-lateral aspect of the cephalic segment of the embryo, and quickly grow into a series of parallel oblique bars, separated from one another by intermediate grooves that show both externally and internally. These grooves are the analogues of the gill slits of the embryos of the lower animals.

But in mammals that have no aquatic stage of development, and breathe by means of lungs,

FIG. 18.—Diagram of the anterior end of a 10 mm. embryo showing the visceral arches. *n,* Nasal pit; *m,* mouth; *md,* mandibular arch; *sp,* auditory groove; *h,* hyoid arch; *gc₂,* second branchial groove; *cs,* cervical sinus. (*Stöhr.*)

no gills ever form, and in such embryos there are no actual separations between the arches, the intervals between them, corresponding to the external and internal depressions being closed by an occluding membrane formed by the apposition of the ectoderm at the bottom of the external furrows, and the endoderm at the bottom of the internal furrows. Upon this point all of the best embryologists are now in accord.

Both the arches and the intermediate furrows have varying degrees of importance in connection with the subsequent development of the tissues and organs of the neck.

The *first arch,* as has already been shown, divides into two branches the lower of which, growing more rapidly than its fellow, forms the jaw, i.e., the inferior mandible, while the upper somewhat later furnishes the substance from which the superior maxillary, malar, and palatal bones arise.

The *second arch* provides the substance from which spring the lesser cornua of the hyoid bone and the associated structures of the hyoid region, while its proximal portion originates the styloid process of the temporal bone and the ear ossicle, the stapes.

The *third arch* originates the greater cornua of the hyoid bone, and is commonly called the posterior hyoid arch on that account.

The *fourth* and *fifth arches* give origin to no important structures, but are soon lost through coalescence with the neighboring tissues.

The *first external furrow*, also known as the hyo-mandibular furrow, becomes obliterated with the exception of its proximal, i.e., its superior posterior portion—which develops into the external ear. The *three remaining outer furrows* engage in no important function and become obliterated, one after the other, beginning above where they are larger. The result is that
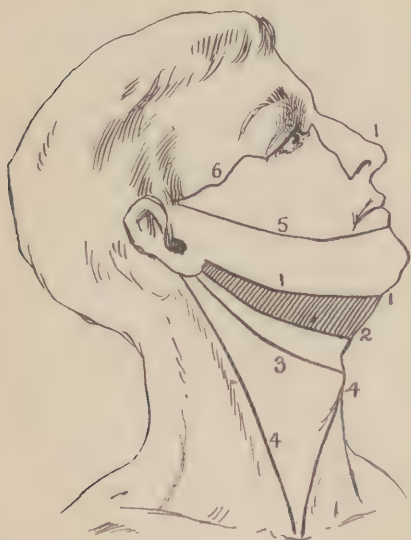
FIG. 19.   FIG. 20.

FIG. 19.—Diagram illustrating Cusset's idea of the position of the branchial clefts and fistulae. 1, 2, 3, 4, The 1st. 2nd, 3rd and 4th clefts; 5, the intermaxillary fissure; 6, the fronto-maxillary or orbito-maxillary fissure; 7, the naso-maxillary fissure. (*Redrawn from Le Dentu and Delbet.*)
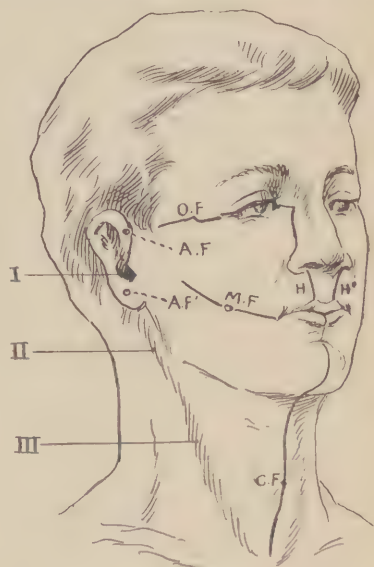
FIG. 20.—Diagram illustrating Sir John Bland Sutton's idea of the positions of the fissures and resulting cysts and fistulae. *AF* and *AF'*, The position of the congenital auricular fistulae; *I, II, III, IV*, positions of the cutaneous orifices of the branchial fistulae; *OF*, orbito-frontal fissure; *M.F*, intermaxillary fissure; *CF* and *CF'*, orifices of mid-cervical fistulae; *H,H'*, labio-nasal fissures, the positions of hare-lip. (*Redrawn from Le Dentu and Delbet.*)

the fourth furrow becomes covered by the fourth arch, the third by the third arch, the second by the second arch, and as each arch is longer than its neighbor as the ascent is made, the broader tissue mass of the upper portion of the neck, comes to overlie the lower, as well as to overhang it on each side above, at the same time that the lower useless fifth arches sink and disappear. Thus an irregular space, the precervical sinus—*sinus precervicalis* of His—is formed on each side of the neck, between the tissues of the neck formed by the arches as described, and those of the thorax below. It is of brief duration, however, as the coalescence of the neighboring parts soon results in its complete disappearance.

The furrows on the inner wall of the developing neck are frequently spoken of as the pharyngeal pouches, and from the embryonal substance of these situations a number of important structures are developed.

Thus, from the first pouch are produced the outer and dorsal portions of the middle ear, the tympanic membrane and the Eustachian tube.

The tissues about the second pouch give origin to no permanent structures, but partly survive as unimportant bulgings, the fossa of Rosenmüller. From the third and fourth pouches, however, are derived the epithelial elements of the thymus gland, and part of the substance of the thyroid and parathyroids.

Before it was so definitely shown that the interval between the visceral arches was closed by the pharyngeal membrane, and everyone believed that in human embryos, as in those of the aquatic animals the arches were separated from one another by clefts, it was easy to account for a fistulous passage between the pharynx and the exterior upon the assumption that development had miscarried to the extent of incomplete closure of one of these clefts. But if there be no such clefts, how can such a communication be effected? There are two theories of cervical or branchial fistula:

I. The original theory of Cusset, supported by J. Bland Sutton, that teaches that upon occasion, at least, there are real branchial clefts in the human embryo, which lay the foundation of the fistula, which results from the failure of development.

II. The theory of Arrou, Fredet and Demorest, who believe that in all cases the fistula is attributable to vestiges of the sinus percervicalis, or conduit of Rabl, and has nothing at all to do with the branchial fissures.

Branchial fistulae are interesting and important lesions about which there is much to be said, but for reasons that will be quite clear hereafter, their consideration will be postponed until the discussion of persistent embryonal structures and the debris resulting from their incomplete absorption, is reached.

III. In the Spinal Region

Spina Bifida or Rachischisis

Spina bifida is a congenital malformation that results from the escape of the spinal cord, or its membranes, or both, through a fissure in the vertebral column.

Except in spina bifida occulta it is recognized by the presence of a tumor over some part of the spinal column of the new-born. It is most commonly situated in the lumbo-sacral, more rarely in the cervical region, almost never in the dorsal region. Its size, form and quality vary in different cases.

The tumor is median, more or less prominent, and either sessile or pedunculated. It is often possible to feel a row of little bony prominences on each side of the tumor. They are the ununited lamina of the vertebra.

The tumor is usually soft, and may be reducible as well as compressible if its cavity connects with the spinal canal. If the communication be free, the tumor may enlarge when the child cries, and diminish when it is quiet. If it be compressed, the child may show the effects of intra-spinous or intra-cephalic pressure, and be thrown into convulsions.

Many cases are complicated with hydrocephalus, and nearly all cases show more or less nervous disturbance varying according to the altitude of the lesion. If low, there are motor and sensory disturbances of the lower limbs, club-foot being one of the more frequent; if higher, additional disturbance in the form of incontenence of feces and urine. Trophic disturbances frequently appear in the form of ulcerations and necroses sometimes quickly followed by infection—

chiefly cerebro-spinal—though not infrequently general, and of course fatal.

The etiology of spina bifida is very simple if the development of the parts be understood.

Upon the dorsal surfaces of very young human embryos the position of the future spinal canal is foreshadowed by the appearance of a longitudinal groove. Externod was able to find it in an embryo only 1.3 mm. in length and probably not more than 12 or 14 days old. Along each side of this groove ridges soon develop into the so-called medullary folds or crests, which rise higher and higher, incline toward one another and eventually unite in the middle line, beginning in the dorsal region, and extending toward the cephalic and caudal ends, forming the *neural* or *medullary canal*.

At first this canal, which is destined to become the central canal of the future spinal cord, is open at both ends. As it is formed by depression and sequestration of the ectoderm, it is lined throughout by ectodermal cells which are the source of the future brain and spinal cord. They at first appear as columnar cells, and in that form their descendents remain in the central canal of the perfected cord.

About the same time that the neural canal is being completed by the arching over of the posterior tissues, a somewhat similar process is in progress on the ventral surface of the embryo in the endoderm. Along its median line a narrow band of cells appears, the edges of which gradually rise, advance towards one another, and finally unite, to form a slender cylindrical structure in the center of which there may be a minute lumen.

In the course of time the lumen is obliterated through multiplication of the cells, and later the cells undergo a peculiar modification by which the whole structure is transformed into a solid elastic rod surrounded by a sheath. This is called the *notochord* and is the primitive axis about which the future spinal column will be formed. It is a temporary structure of which the only vestiges that remain in later life are small bits of pulpy substance occasionally to be found in the centers of the intervertebral discs of the spinal column.

The developing spinal cord at first extends along the entire length of the medullary canal, down to and including the coccyx, but as time goes on, the development of the cord progresses more slowly than that of its bony encasement, and the vertebral column outgrows it to such an extent that at the time of maturity the spinal cord occupies the spinal canal only as far down as the interval between the first and second lumbar vertebra.

The spinal column is successively membranous, cartilaginous and osseous. The membranous structure is first formed from three mesodermic expansions, of which the two anterior surround the notochord, and the third or posterior forms behind it. Cartilage first appears about the middle of the second month, simultaneously in the bodies and lateral processes of the vertebrae, which are, at this time represented by arches with the concavity directed posteriorly. These arches develop into the individual vertebrae by a very complicated series of events, and from various centers of ossification, but for present purposes it is sufficient to understand that they continue to extend posteriorly, forming first the pedicles by which the sides of the spinal cord are protected, then the lamina by which the posterior surface is covered, and from which the spinous processes are finally developed. The spinal canal is surrounded by its bony incasement by the fourth or fifth month, but complete ossification is delayed until long after birth.

If the formation of the lamina during the fourth month be in any way arrested, the posterior inclosure of the spinal canal remains imperfect, and spina bifida is the usual result.

But, as in the case of the arrested development of the face and neck, it does not explain the condition. Spina bifida results from an arrest of development, but the cause of that arrest is unknown. There are, however, several theories about it, which Proust sums up as follows:

1. The presence of amniotic adhesions. The frequent appearance of a cicatrix upon the surface of the lesion, is supposed to be in favor of this theory.

2. The presence of a tumor—*medulloma*—in the medullary canal, by which its posterior closure is prevented.

3. The occurrence of limited spinal dropsy, by which a certain level of the cord is kept unduly distended.

4. Arrested development of the posterior arches, by which the spinal canal should be closed

Of these Proust favors the last, and supports his view with the following reflections:

1. The frequency of spina bifida in the dorso-lumbar and lumbo-sacral regions is explained by the late obliteration of the neural pore and rachidian groove at those points.

2. The discovery of spinal cord tissue or its vestiges in spina bifida of the lumbar and sacral regions, which is due to the greater length of the foetal cord.

3. The integrity of the cord in certain cases, which depends upon the fact that the closure of the medullary groove takes place earlier than that of the vertebral column.

4. The coexistence of a medullary fissure with a rachic fissure in the most serious cases, that arise during the very early stages of embryonal development, before either the spinal cord had been formed or the canal closed.

The malformation has long been recognized, though not until recently understood. A description of it is said to be contained in the writings of Tulpius, (1672). Observations upon it were made by Morgagni, and by Ruysch. Embryological studies were made by Darest, and by Tourneau and Martin. Other important contributions have been made by von Recklinghausen, Muscatello, Vurpas and Uschide, de Rabaudaud, Lapointe, and Denuce.

Nearly all later writers have more or less completely adopted the classification of von Recklinghausen:

    I. Meningocele.
   II. Myelocystocele.
  III. Myelomeningocele.

But that there are difficulties in the way of satisfactorily classifying cases is shown by Woltman who studied 187 cases observed in the Mayo Clinic, that he declined to classify at all.

Okinczyc observes that "Rachischisis being the constant element in spina bifida, the classification is necessarily based upon the variable ones, that is to say, the medullary and meningeal malformations in their varying degrees. If we pass from the most simple to the most complex, we encounter the following:

I. Rachischisis without malformation either meningeal or medullary, or at least very slight malformation—*Spina bifida occulta.*

II. Rachischisis associated with meningeal malformation, but with a normal spinal cord. It is characterized by a fluid distension of the meninges. If this be behind the cord, it gives rise to a pure *Meningocele;* if it be front of the cord, elevating it and stretching it over the cyst, it is a *Myelomeningocele.*

III. Rachischisis associated with medullarly malformation, the medullary canal being closed, but the central canal cystically distended—*Myelocystocele.* Of this there seem to be two varieties: a pure form in which there is no associated meningocele, and a complicated form—*Myelocystomeningocele.*

IV. Rachischisis associated with myeloschisis (Lapointe). It is a rare, complicated and grave variety in which there is a fissure in the spinal column associated with a fissure in the cord. Von Recklinghausen regards these as extreme cases of Myelomeningocele, and in this view Okinczyc concurs.

The rachischisis that is the foundation of spina bifida may be anterior, posterior or lateral. It may also be partial or complete. It is usually partial and posterior.

I. Spina Bifida Occulta

In these somewhat rare cases that occasionally pass undetected, there is no tumor to direct attention to the spinal region, and the child at birth may pass for normal, and continue to be so regarded until certain nervous symptoms present themselves. It may be then that the first careful examination of the dorsal surface of the body is made, and a more or less well marked and conspicu-

Fig. 21.—Hypertrichosis over a spina bifida occulta.   (*Woltman.*)

ous area of hypertrichosis found in the lumbo-sacral region. By careful palpation of this area any existing vertebral fissure may be detected in the form of a groove, on each side of which, like a string of beads, a row of little osseous projections can be felt. They are the tips of the bony projections whose normal backward prolongation should have formed the lamina and spinous processes of the vertebrae. The degree of bony defect is variable and sometimes takes peculiar form, as in a few cases in which there were pseudarthroses between the partly formed lamina, and their seat of origin. In the not infrequent cases in which the osseous defect is associated with a centrally situated lipoma it may be impossible to discover the position of the bony defect.

In spina bifida occulta there is usually no primary disturbance of the cord, but if the bony defect be associated with conditions that effect pressure upon it,

attention is soon directed to the spinal region by pain, and other nervous symptoms.

Such pressure has numerous causes, and through anatomical dissection it has been determined that it sometimes is referable to the relics of antecedent healed myelocystocele sometimes to the presence of retromedullary tumors originating in the debris of the sclerotomes, or of the neural crests, as they not infrequently contain ganglionic nerve cells derived from the latter.

FIG. 22.—Sacral dimple (fovea sacralis), a very significant defect in spina bifida.   (*Woltman.*)

II. Spina Bifida Cystica

1. *Meningocele.*—This form of spina bifida was at one time regarded as common but is now known to be rare. It is superficially recognized by the fact that the skin is always continuous over the surface of the tumor. The dura mater, according to both von Recklinghausen and Muscatello, is always lacking behind, where it reaches only to the limits of the bony arch.

The other membranes, the pia and arachnoid, however, are continued over the surface of the tumor, though they present a kind of embryonal appearance and are distended by fluid that presses them back at the periphery, outside of the spinal fissure so as to form a sessile or pedunculated cyst.

2. *Myelominingocele* or *Myelocele.*—This is said by Babcock to be the most frequent variety of the malformation. It differs from the previous form in that the cystic accumulation is anterior to the cord, which is elevated, thrust through the fissure in the vertebral arches, stretched and compressed, its columns frequently being separated and partly distributed.

Meningocele

Myelomeningocele

Myelocystocele

Myeloschisis, the most grave variety of the malformation.
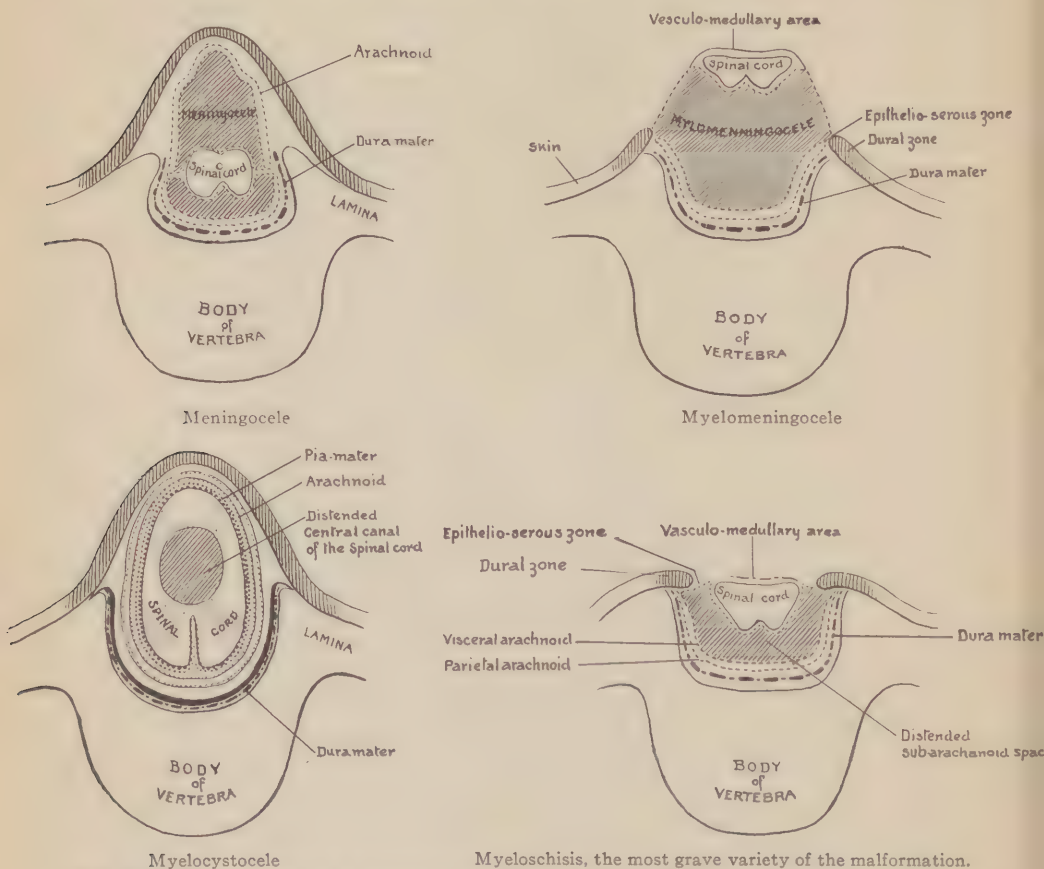
FIG. 23.—Diagram showing the conditions obtaining in the different varieties of spina bifida. (*Redrawn from Forgue.*)

3. *Myelocystocele—Myelocystomeningocele.*—These cases arise after the closure of the medullary groove, and result from distension of the central canal, by which the posterior portion of the cord and its covering membranes are forced through the rachic fissure. All parts of the cord may be affected, but the anterior and posterior commissures, being the regions of least differentiation suffer most commonly. This form of spina bifida may take place either anteriorly or posteriorly, more frequently the latter. It may also occur in the cervical region, and the tumor formed is not infrequently multilocular. The covering integuments are usually normal in appearance, though a bluish translucent membrane sometimes appears in the central zone, and may be surrounded or covered by what seems to be granulation tissue. In rare cases this internal hydrorrhachis,

constituting the myelocystocele is accompanied by an external hydrorrhachis or meningocele, thus forming a more complicated condition that may be described as *myelocystomeningocele*.

4. *Myeloschisis.*—This form of spina bifida is the result of arrested development of the medullary canal at a very early period, the lower part not becoming covered by the approximated neural crests. Total myeloschisis, which is incompatible with life has no surgical interest, but partial myeloschisis with which the
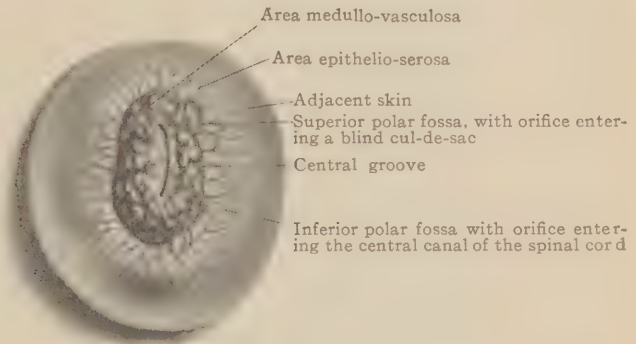
FIG. 24. Gross appearance of the form of spina bifida known as myeloschisis, showing the characteristic structures. (*Redrawn from Okinczyc.*)

child may live for some time is a condition about which the advice of the surgeon is frequently sought. It may occur in the cervical or dorsal region in rare cases, but it is overwhelmingly more frequent in the lumbo-sacral region.

It is characterized by the presence at the time of birth of a very prominent globular tumor over the lower part of the spine. This is particularly large when, as not infrequently happens, it is associated with meningocele. It has much the appearance of granulation tissue but is grayer and more pulpy. Its center is creased by a median longitudinal groove, which shows a tiny opening at the superior and inferior ends. If a probe be introduced into the superior of these, it will be found to enter a blind cul-de-sac; but if it be introduced into the lower one, it enters the ependymal cavity or central canal of the spinal cord. Over the center of the tumor there is a concentric zone of bluish gray, translucent, pearly tissue, over which small vessels ramify in a serpentine fashion, and about it is a circle of very thin skin. The central area is known as the *area medullo-vasculosa* or medullary area; the circle about it as the *area epithelio-serosa* or meningeal area; and beyond it is a third, the *area dermatica* or cutaneous area. The probable origin of the tissues of each of these different areas is indicated by its name. It is not rare to see the skin tending to grow either as a thin layer, or as extending islands from the periphery toward the center as if to cover the meningeal area. In this is seen a tendency toward the spontaneous recovery of the condition through cutaneous cicatrization.

This lesion presents itself in two varieties:

A. Myeloschisis without meningocele. In these cases hypertrichosis in the form of a hairy collar is frequently seen about the tumor. The dura mater assists in covering the posterior surface of the lesion, but beyond the borders of the vertebral groove, is

continuous with the other meninges and the skin encroaching upon them, in the form of a *membrana reuniens*. The roots of the spinal nerves and rudiments of the dentate membranes may be visible. The only recognizable nervous elements appear in the form of a medullary network, and the spinal cord always remains completely open. When the lesion is studied with the microscope, the ependymal cells are found to be continuous with the skin without the presence of any transitional cells. Indeed there is scarcely any true ependyma, except in scattered islets, all having been destroyed. The exposed spinal cord is open behind. Cells of the anterior and posterior horns may be found but the structure of the cord is always greatly confused through the formation and penetration of newly formed vessels under the influence of the associated inflammation.
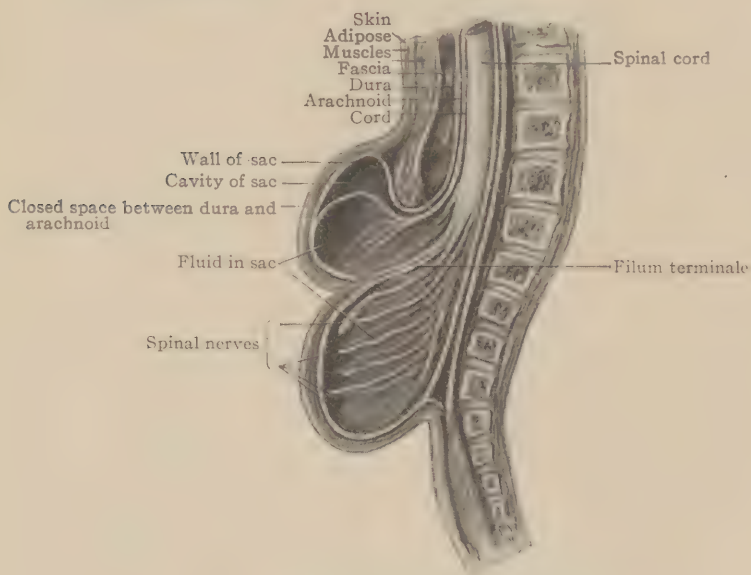
FIG. 25.—Lumbo-sacral spina bifida. (*Virchow.*)

B. Myeloschisis with meningocele. In these cases there is a prominent tumor, except for which the previous description fairly well applies, especially with respect to the histology. There are no muscular elements in the coverings of the tumor, the dura mater never forms behind the spinal cord; only the pia participates in the formation of the meningocele. The membrana reuniens forms a kind of chorion.

Tourneaux and Martin have described a "closed myeloschisis," but Okinczyc notes that the terms are contradictory, as the word myeloschisis means that the central canal is open. He suspects an error in the interpretation of their case, in which the lesion may have become closed through secondary cicatrization. If that be true, there may be such a thing as the healing of these lesions in utero.

It is not easy, and it may not be possible to make a clinical differential diagnosis of the varieties of spina bifida, which is unfortunate as they differ greatly in severity, fatality, and remediability by surgical intervention. But in general it may be stated that the prognosis is bad, and most of the children die early. The tumor badly protected by its coverings of embryonal tissue, is almost certain to become infected, and to ulcerate with subsequent rupture and escape of cerebro-spinal fluid.

If that does not occur, the infection is apt to be transmitted to the cerebral meninges with consequent fatal meningitis or hydrocephalus.

The prognosis is best in spina bifida occulta, in which there is no disturbance of the spinal cord, and no unprotected tissue. It is probably next best in meningocele, especially if there be no communication between the sac and the spinal cord.

The surgeon should not feel that the case is hopeless if there be such a communication, however, as it is sometimes quite possible to remove the sac,

FIG. 26.—Double spina bifida cystica in the cervical region. At operation the lower cyst was found to contain a dermoid. (*Woltman.*)

suture the membrane, provide an artificial bony support, and maintain the child in a semi-reversed position until the wound has closed and the new bone united with the surrounding osseous tissues. The appearance of hydrocephalus, however, whether it come early or late is a very unfavorable sign.

Spina bifida in the sacral region seems to merit special mention on account of the tumors with which it is not infrequently complicated.

Proust recognizes two varieties:

I. Spina bifida occulta or spina bifida latenta.

This form of malformation is very rare in the sacral region. The bony defect is completely closed posteriorly by a fibrous membrane through a perforation in which a band of fibro-cellular tissue passes to connect the skin above with a tumor in the

vertebral canal. This tumor, which surrounds the inferior extremity of the spinal cord, is usually badly circumscribed, composed of fibrous, muscular and adipose tissue and develops from developmental disturbances prior to the time when the spinal cord begins its ascent in the more rapidly growing spinal canal. The associated tumors are not always in the spinal canal; sometimes they lie between the membrane closing the defect and the skin above. Under these circumstances the tumor is usually composed of adipose tissue or of a mixture of adipose and fibrillar tissues. It may obscure the diagnosis of the true condition, by interposing a soft cushion between the chief diagnostic feature, the double row of bony eminences, and the palpating finger. But in all cases in which there are unaccountable nervous symptoms such as persistent pain in the back, club foot, incontenence of urine or feces, the condition should be suspected, and if the physical examination of the patient reveal hypertrichosis in the sacral region, or show a superficial cicatricial area, or the presence of a tumefaction of soft consistence or an actual tumor, a more thorough examination with the X-rays is indicated.

II. Complicated spina bifida. In these cases of developed spina bifida, the walls of the sac, both membranous and cutaneous are totaly or partially hyperplastic or neoplastic in such manner that new formations resembling angioma, lipoma, fibroma or myxoma, mask the appearance of the lesion, making its recognition difficult, and sometimes impossible.

Proust thinks it highly probable that a considerable number of spina bifidas actually recover, separating themselves from their connections with the spinal canal by pedicles which become more and more slender until they finally rupture as the osseous tissues close behind them. And he supposes that many of the peculiar tumors occurring about the inferior extremity of the spinal column originate in the embryonal structures thus isolated. He thus accounts for sacro-coccygeal lymphangiomas, whose multilocular cystic spaces with endothelial linings represent the vestiges of the cavity of the arachnoid, or the dural lymphangiectasias of an old meningocele. He does not, however, attribute to this origin the mixed tumors of the region which, as will be later explained, are derived from a different source— see the section upon the congenital conditions depending upon the debris of obsolete but incompletely absorbed embryonal structures.

IV. In the Ventral Region

Thoracoschisis

The thoracic and abdominal walls are the result of the forward growth and final coalescence of the somatopleurs in the middle line anteriorly. If the fusion fail in the thoracic region, thoracoschisis results; if in the abdominal region, gastroschisis.

Thorachoschisis usually occurs in the form of *fissura sterni*, which is a defect of varying size and depth. When complete it is apt to be complicated with *ectopia cordis* or as it is also called, "pectoral heart."

If the defect in the coalescence of the somatopleur is accompanied by a similar defect of the splanchnopleur, the ectopic heart is without a pericardium; if the splanchnopleur does not participate a pericardium may be present. In either case the malformation is incompatible with life, and the infants usually die in the course of a few hours or days.

Gastroschisis

Defective development of the abdominal wall commonly centers about the umbilicus, the formation and closure of which are complicated and not com-

pleted until a late period. One of the most intelligible accounts of the forma-
tion of the umbilicus, that we have read is that in Heisler's "Textbook of
Embryology."

"After the splitting of the parietal plate of the mesoderm into its two lamellae, and the union
of the outer layer with the ectoderm and the inner with the endoderm to form respectively the
somatopleure and the splanchnopleure, these two double layered sheets undergo folding in
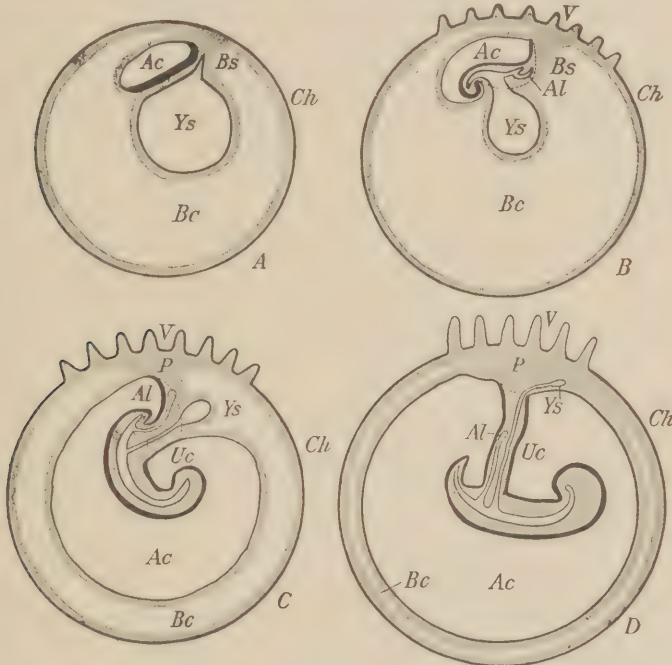
FIG. 27.—Diagram illustrating the formation of the umbilical cord. The heavy black line
represents the embryonic ectoderm; the dotted line represents the line of reflection of the body
ectoderm into that of the amnion. *Ac*, Amniotic cavity; *Al*, allantois; *Bc*, extra-embryonic
coelom; *Bs*, belly-stalk; *Ch*, chorion; *P*, placenta; *Nc*, umbilical cord; *V*, chorionic villi; *Ys*,
yolk-sac. (*McMurrich*.)

various directions. Before the folding occurs the germ is a hollow sphere whose cavity is the
archenteron and whose walls are the somatopleure and the splanchnopleure. While the
somatopleure in a zone corresponding to the margin of the embryonic area becomes depressed
and is carried under that area to form the lateral and ventral body wall of the embryo, and also
more distally folds up over the area to produce the amnion and the false amnion, the splanch-
nopleure, likewise in a line corresponding with the periphery of the embryonic area, is depressed
and carried inward from all sides towards the position of the future umbilicus. The folding in
of the splanchnopleure effects the division of the archenteron into two parts, a smaller cavity
falling within the body of the embryo, which latter is forming at the same time, and a larger
extra-embryonic compartment, which is the yolk-sac or umbilical vesicle. The intra-embry-
onic cavity is the gut-tract. The constricted communication between the two is the vitelline
duct. While the vitelline duct is still a rather wide aperture, the anterior and posterior parts
of its intestinal orifice are designated respectively the anterior and posterior intestinal portals.
As the somatopleure closes in around the vitelline duct it forms the wall of the abdomen, the
opening left, which is traversed by the duct, being the umbilical aperture.

"Another structure, the allantois, makes its appearance about the time the somatopleur
begins the division of the archenteron into the vitelline and gut cavities, in the form of an

exvagination or diverticulum from the posterior part of the future gut and is excluded from the future body cavity by the forming abdominal wall just as the vitelline cavity is. There are, therefore, two separate structures about which the future abdominal wall forms, and which remain for a time projecting through the primitive umbilicus by narrowing pedicles.

" Both are destined to entirely disappear by shrinkage and atrophy as the chorion develops into the placenta and the belly-stalk becomes penetrated by its vessels. Through arrest of development, however, their disappearance may be retarded, and a vestige of the vitelline duct may survive in the form of a connection between the intestine and the umbilicus, *Meckel's diverticulum*, and a vestige of the allantois between the bladder and the umbilicus, the *urachus*."

But the development of the parts has been followed no further than the third week, and the abdominal wall is far from completed. If at that time a careful examination of the part be made, an opening would be found in the abdominal parieties, in which, one above the other were two smaller ones. Forgue describes the former as the "cutaneous umbilicus," the latter as the "intestinal umbilicus" (above), and "urinary umbilicus" (below) respectively. In the further development of the abdominal wall, the cutaneous umbilicus constricts, the intestinal and urinary umbilici contract, and the portion of the somatopleure that gives rise to the peritoneum, forms a compact dorsal layer, and a thin membranous ventral layer—the *membrana reuniens*—that closes the intervals in the cutaneous umbilicus, while the mesodermal elements of which it is composed are transforming it into peritoneum on the inside, and providing muscle between the two layers on the outside of the primitive abdominal wall. By the time that the developmental processes have closed the intestinal and urinary openings, the original abdominal umbilical opening has disappeared through the perfection of the cutaneous and aponeurotic tissues of the abdominal wall on the outside and the peritoneum on the inside.
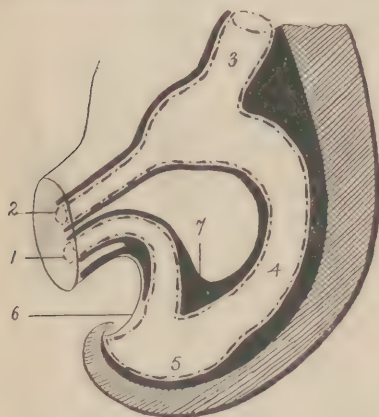
FIG. 28.—Median section of an embryo, showing the structures that form the umbilicus. 1, Pedicle of the allantois; 2, pedicle of the umbilical vesicle; 3, foregut or primitive intestine above the umbilicus; 4, hind-gut or primitive intestine below the umbilicus; 5, cloaca interna; 6, anal membrane; 7, perineal spur. (*Redrawn from Vailleton.*)

There are three principal miscarriages of these developmental steps (1) The cutaneous umbilicus may not close, whereupon the abdominal viscera tend to prolapse through the weak point in the abdominal wall—*congenital umbilical hernia*. (2) A vestige of the vitelline duct may remain—*Meckel's diverticulum*. (3) A vestige of the allantois may remain—*patulous urachus*. But these are not all; fragments or vestiges of any of the tissues taking part in the formation of the various stages in the development of the umbilici may remain and form the starting point of neoplasmic masses appearing later.

At this point only one of these defects will be considered, the others being reserved until the section dealing with the persistence of the debris of absolute and incompletely absorbed embryonal structures is reached.

Congenital Umbilical Hernia

Congenital umbilical hernia is the complete or partial escape of some of the abdominal viscera through an imperfectly closed umbilicus.

The umbilicus of the infant is probably always the weakest part of its abdominal wall. Scarpa long ago observed that if traction was made upon the

umbilical cord, a deep thimble-like depression in immediately formed on the inner wall, and that if the tip of the finger be slightly pressed against the inner wall just below the umbilicus of the new-born, a similar projection can be produced.

Recalling the development of the umbilicus it is easy to understand that the younger the fetus, the weaker its umbilicus will be, and the younger the embryo the larger the umbilical opening will be. From this it results that the largest hernias are usually developed most early. But the size is not the only feature indicative of the age of the lesion. If the protrusion of the viscera begins early, the sac may be composed of embryonal tissue, if later of fetal tissue. According to the quality of the sac, therefore, Duplay has made two subdivisions of these hernias:

1. *Congenital Embryonal Hernia.*—This develops before the third month and is characterized by a sac composed of the original undifferentiated membranous wall of the primitive abdomen, the *membrana reuniens.*

2. *Congenital Fetal Hernia.*—Which arises after the third month and hence after the abdominal wall has formed. Its sac is composed of peritoneal tissue.

Here it should perhaps be stated that the most complete form of *ectopia visccrorum* differs considerably from umbilical hernia in origin.

The formation of the viscera of the embryo is in progress upon the under surface of the embryonic disc as the somatopleur and splanchnopleur extends to surround and cover them. If the growth of these layers be arrested at a very early period, there will be no abdominal wall, and the viscera will develop, so to speak, outside of the body. This is not umbilical hernia, for there is not, and never was, an umbilicus through which the viscera could prolapse. But when the advance of the somatopleur and splanchnopleur has completed the formation of the abdominal wall except at the central opening, then the term umbilical hernia becomes appropriate.

From this it will be seen that the appearance presented by different cases of congenital umbilical hernia must vary according to the time at which the defect developed.

When such a lesion is extremely small it may entirely escape detection and its presence first be observed when the ligated umbilical cord detaches. This is because the portion of the bowel contained in the hernial sac being caught in the ligature and strangulated, its distal destroyed tissue separates with the falling cord and leaves a fecal fistula. It will, of course, occur to the reader that it could not have been the entire intestine that was thus ligated, or the child must have died of intestinal obstruction prior to the separation of the cord. Such a condition only supervenes, therefore, when a pucker of the intestinal wall is caught and held.

Larger hernias appear at the time of birth as globular or pyriform swellings at the implantation of the umbilical cord. They may be centrally situated extending into the tissues of the cord and covered by its vessels which sometimes give a lobulated form. Or, they may be situated at one edge of the attachment of the cord and seemingly independent of it. The size varies, but they are not usually larger than a walnut or billiard ball. The coverings are transparent,

corresponding with those of the cord, and they are usually easily reducible. The sacs of these hernias vary in structure. In many they are composed of a transparent membrane through which blood-vessels plentifully ramify, in others of a slightly more delicate membrane without any. The former is the peritoneum, the latter the embryonal *membrana reuniens* or primitive membrane of Rathke. The sac is usually very fragile, is continuous with the sheath of the cord on the one hand, and with the integument on the other. Between the two there is usually a plentiful collection of the jelly of Wharton. The whole thing is thus quite transparent, and through its tissues the intestinal loops, or other contents can be seen.

The fetal hernia should be easily recognized by the fact that it is covered by the finished, though weak abdominal wall. It is usually not large, and it usually contains only a single loop of the small intestine. The force determining the displacement is unknown. Forgue seems to incline toward the opinion that malposition of the fetus in utero may be to blame.

For the large embryonal hernias nothing can be done; small ones may disappear spontaneously through the final but delayed completion of the abdominal walls; most cases require some kind of surgical intervention.

Ectopia Vesicae

When the abdominal fissure extends below the umbilicus, or involves only the tissues of the lower anterior region, a very rare deformity, the bladder sometimes prolapses through the opening. Such a case has been reported by Froriep and Gusserow, but doubt as the precise anatomical relations seems to exist, and Kirmisson looked upon it as a prolapse of the posterior wall of the bladder through a urinary fistula at the umbilicus. However that may be, the deformity must not be confused with the next to be discussed, which is essentially different.

Exstrophia Vesicae

This is a congenital malformation characterized by the occurrence of a fissure in the anterior inferior abdominal wall through which the inner surface of the posterior wall of the bladder projects.

At first glance it seems to result from arrested development of the abdominal wall, and for that reason appears at this point in our classification; but if the malformation was no more than that, the whole bladder should prolapse, and the deformity would be ectopia vesicae. That which chiefly characterizes the condition, and makes it exstrophy, is absence of the anterior wall of the bladder.

It is referable to an arrest of development taking place very early, and affecting not only the anterior abdominal wall, but various other structures of the posterior extremity of the embryonal body. It is a rare malformation, that occurs according to Puesch once in one hundred thousand births, according to Neudorfer once in fifty thousand births. It is more frequent in males than in females, the proportions usually given being 6:1. It does occur, therefore, in both sexes, in all grades.

Three clinical varieties of the malformation are commonly described though with very little justification.

I. *Complete Exstrophy.*—In this form the umbilicus appears to be situated abnormally low down, to be of an unusual crescentic shape—the concavity of the crescent being below—and to have its vessels spread out laterally. Below the umbilicus the abdominal wall is defective, the skin terminating rather abruptly in a median projecting area of red color and mammillated appearance, covered with glairy mucus. It is the posterior wall of the bladder, and low down upon its surface the

FIG. 29.—Exstrophy of the bladder in a little boy. Observe the absence of an umbilicus, the dark colored mucosa of the posterior vesical wall just above the deformed penis with epispadias. (*From a photograph of a patient of Dr. James A. Kelly's.*)

two little orifices of the ureters can be seen occasionally ejecting drops of urine. The whole of this area is thrust forward by the pressure of the intestines behind. No attempt at reduction and replacement can be successful because the condition is not the result of displacement of the bladder so much as absence of its anterior wall and suprajacent structures. Descending toward the pelvic region it is soon discovered that there is no symphysis pubis, the pubic bones being separated from one another, and the pelvis flattened in consequence. There may be no urethra. In males the lower part of the open bladder terminates in a groove upon the dorsal

surface of the dwarfed and deformed penis—epispadias—the scrotum is malformed, and the testes frequently extopic.

The ejaculatory ducts open into the urethral gutter, and no trace of either a prostate or of seminal vesicles can be found. In very rare cases a vesicle anus, i.e., an opening by which the rectum communicates with the bladder, may be present.

In females the clitoris may be bifid, and the labia and nymphae atrophic. The urethral gutter opens into the vestibule.

II. *Inferior Vertical Fissure.*—This more rare form of the deformity seems to occur in females only. It may not at first be recognized as exstrophy, as the fissure passes below the intact symphysis pubis to establish a communication with the bladder
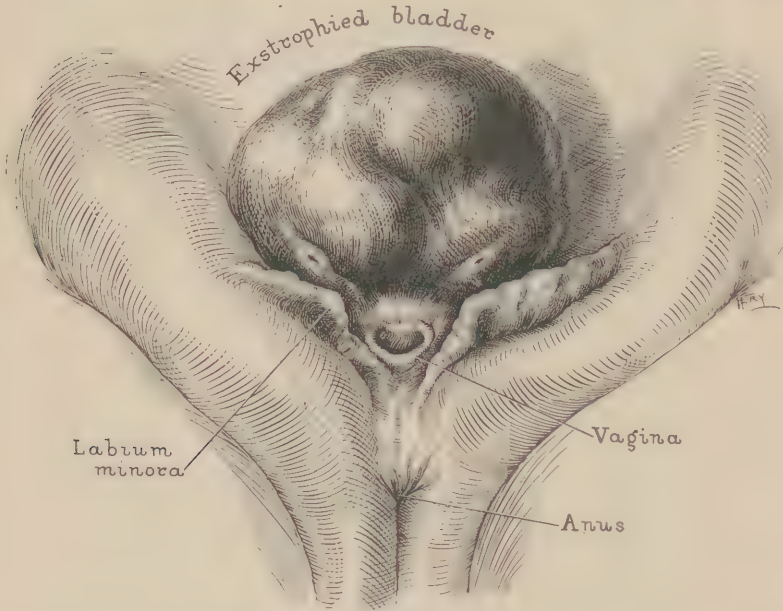
FIG. 30.—Exstrophy of the bladder in a little girl. The ureteral openings show very distinctly on the exposed mucous membrane of the posterior vesical wall. (*C. H. Mayo.*)

along the posterior part of the urethra. The clitoris is always bifid, but the uterus and vagina are single. The urine trickles from the posterior part of the urethra. The condition closely resembles epispadias in the female, with which it is always associated, but differs from it in that the anterior part of the urethra is always intact.

III. *Superior Vertical Fissure.*—This is another rare form of exstrophy in which the fissure is above the well-formed symphysis pubis, in the neighborhood of the umbilicus. It seems to be closely connected with or related to the vesico-umbilical fistula that follows persistence of the urachus. Such cases have been observed by Coates, Rigaud, Froriep, and Braun. In those reported by Coates and Rigaud there was a circumscribed orifice in the linea alba through which the posterior wall of the bladder projected. In Coates case the urethra terminated in a cul-de-sac beside the bladder, the vagina being inperforate. In Rigaud's case also, the bladder did not communicate with the urethra though the genital organs were normal.

Cases of exstrophy of the bladder are rarely exactly alike, and it seems probable that if they could be collected and placed in series passing from the most severe to the most mild, the exstrophy and length of the abdominal

fissure would be found to diminish, the interval between the umbilicus and the exstrophy becoming greater, the length of the fissure in the bladder shorter, and the separation of the pubic bones narrower, until there ceased any longer to be an abdominal lesion, and remained only a guttered penis or clitoris opening by a wide orifice into the neck of the bladder which lacks a constrictor muscle. When such a point is reached, it becomes difficult to be sure that it is not epispadias.

To understand and explain the conditions it becomes necessary to review the embryological development of the parts.

In the third week of embryonal life, at the same time that the growth of the somatopleur is beginning to divide the primitive archenteron into the primitive gut cavity and the vitelline sac, and the allantois is sprouting as a diverticulum from the primitive gut, the posterior or tail end of the embryo is curved anteriorly. It contains a number of structures viz., the medullary canal, the chorda dorsalis, and a part of the developing intestine known as the post-anal gut. On the middle of the ventral surface, a short distance from the top of the tail, the ectoderm and entoderm push aside the growing mesoderm, and form a thin area known as the *anal plate*, which corresponds with the position of the future anus which as yet does not exist as an opening. As the umbilicus develops and the vitelline duct and allantois are drawn together, the tail process becomes straightened out and less distinct, and the anal membrane drawn backward to a position corresponding to that of the future perineum, where it occupies a depression, the *anal pit*, or *proctodeum*. Later, this anal membrane with which we are to be most concerned in the pursuit of the cause of exstrophy of the bladder, undergoes considerable thickening and forms the *anal plug*. This soon divides into two distinct portions, the posterior, which is destined to excavate an opening into the intestinal canal, the anus, and the anterior, which moves forward and is destined to excavate another into the sinus uro-genitalis during the formation of the urinary and sexual organs.

If the inferior part of the developing abdominal wall be carefully examined at this time, it may be found composed of two parts. One of these lying immediately below the umbilicus being formed of the united somatopleures, the primitive abdominal wall, the other, lower down, of the anal membrane. For present purposes let the posterior segment of the anal membrane or plug be neglected and attention directed to its anterior portion. It can be imagined that in case of an arrest of development of the anterior part of the abdominal wall, the anal membrane might be pushed up toward the umbilicus to a point corresponding with the extent of the disturbance, even at times to the umbilicus itself. As it is the function of the anal membrane to disappear through the formation of an opening, it is easy to understand that if detained in its abnormal position until time for this function to be manifested, there will inevitably result a defect in the abdominal wall corresponding with the part closed by the anal membrane, associated with abnormally large openings into the urinary and sexual outlets. Such is the explanation given by Veilleton.

No theory yet advanced has been able to explain all of the facts of exstrophy of the bladder, but the embryological theory advanced explains the greatest number. Thus, if the anterior portion of the anal membrane whose function it is to open a passage-way into the uro-genital sinus be slightly extended forward, it increases the size of the opening and advances it anteriorly to a point at which the perfection of the formation of the urethra by the appropriate structures becomes impossible, and epispadis, which, for the sake of argument may be regarded as the first degree of exstrophy, takes place. If for any reason it be pushed still further forward, the dehiscence will be correspondingly increased in a forward direction, and the neck of the bladder opened. Still further forward extension will increase the dehiscence until in its most extreme degree the entire

abdominal wall below the umbilicus will be involved and the entire anterior wall of the bladder be missing as well as the symphysis pubis unformed.

Cases of exstrophy of the bladder may die early, the exposed vesical mucosa becoming inflamed and the infection ascending to the kidneys. Vigneau followed 71 cases and found that 10 died before the 10th year, 15 between the 20th and 40th year and 5 between the 40th and 50th years. One case lived to be 70 years old.

FIG. 31.—Adenocarcinoma covering the left half of the exstrophied bladder. The ureteral orifices at the base of the bladder are not involved in the malignant area. (*Scholl.*)

Women with exstrophy of the bladder have been known to bear children, but the sexual life of males is interferred with because of the associated epispadias, the superficially placed and exposed ejaculatory ducts, the absence of seminal vesicles, the absence of the prostate gland, and the short length and peculiar shape of the penis.

The symptom causing the greatest distress to the patient is the persistent and irremediable incontenence of urine.

But aside from this annoyance there is always the danger that the persistent irritation of the tissues by the dribbling urine may effect malignant growth on the part of vestigial embryonal tissue sequestered in the lesion. To this Scholl has recently called attention, and in proof of the potential malignancy of the

condition has collected nine cases in which there were either carcinoma or changes that might be supposed to predispose to them. Out of 367,000 patients at the Mayo Clinic, there were 69 with exstrophy of the bladder, in three of which there was malignant disease, always adeno-carinoma.
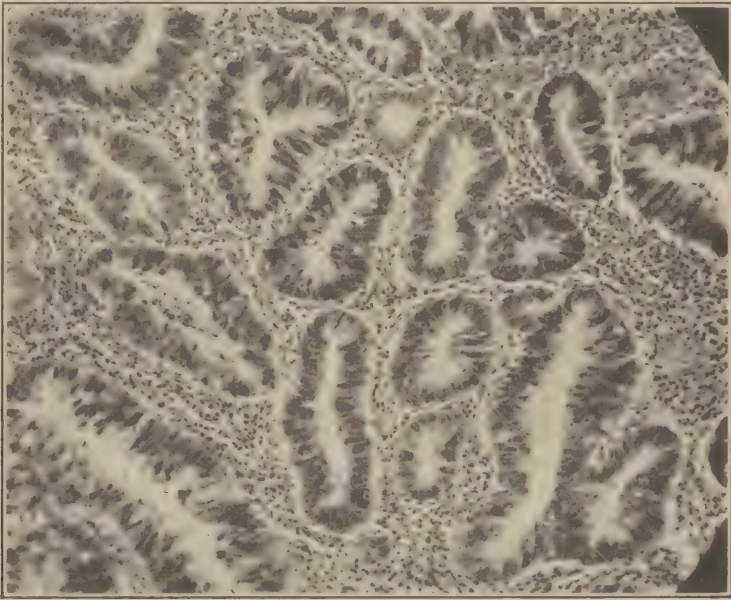
Fig. 32.—Type of malignant structure found in the exstrophied bladder of a man aged forty-four years (×100). (*Scholl.*)

V. In the Genital Region

Epispadias

Although it may be regarded by some as a malformation of an organ of sex, it seems logical to consider epispadias at this point because exstrophy is a median fissure of the anterior wall of the bladder, epispadias a median fissure of the anterior wall of the urethra.

It is rare and may occur in either sex, though overwhelmingly more frequent in males.

Its embryological explanation is easily comprehended by those that have read the theory of exstrophy of the bladder as presented in the preceding section of this work. All that is necessary is to consider the possible varying positions of the anal plug, and the conditions arising from them. If it be abnormally advanced toward the umbilicus, exstrophy of the bladder with a long fissure may result; if less advanced, exstrophy with a moderate fissure; if still less advanced, exstrophy with scarcely any external fissure; if very slightly advanced, no opening into the bladder, but division of the anterior wall of the urethra—*epispadias*. Vailleton sums up the whole matter thus: "If there be excessive development of the anal plug, the two halves of the genital tubercle cannot

unite in the median line, but remain separated above, and thus epispadias comes about."

The clinical manifestations vary according to the sex of the individual and to the variety of the malformation.

Fig. 33.—Epispadias in a little boy of 11 months.　(*Redrawn from Kirmisson.*)

I. *Epispadias in the Male Sex.*

The chief characteristics as summarized by Kirmisson are: small size of the penis, exuberance of the prepuce on its inferior surface, and a more or less broad gutter on its anterior surface. The patients are troubled by more or less incontinence of urine. Some hold it only upon effort, some cannot hold it at all. Excoriations and eruptions follow. In adult patients coitus is difficult because of the small size of the penis, and procreation impossible because the sperm cannot be introduced into the female parts.

Forgue divides the cases into three groups:

　　　1. Balanic epispadis
　　　2. Penile epispadias
　　　3. Peno-pubic epispadias

In order to continue the relation between epispadias and extrophy of the bladder, these will be considered in the reversed ordered:

1. *Peno-Pubic Epispadias.*—This is the most common form and that which best connects it with exstrophy of the bladder. It is sometimes spoken of as complete epispadias, and is characterized by an urethral gutter that occupies the entire length of the dorsal surface of the penis which is shorter than normal, more or less retracted, sometimes recurved, and not infrequently twisted. To make a satisfactory examination it is necessary to draw the organ down firmly and spread its tissues out. Narrow at the meatus, wider at the fossa navicularis, the urethral gutter continues backward until it is lost in the infundibular space, bounded above by a kind of cutaneous arch whose extremities unite with the roots of the penis and scrotum. The urethral orifice is found at the bottom of this funnel and is sometimes large enough to admit the tip of the finger. The urethral mucosa with which the gutter is lined, deepens in color as the bladder is approached. The glans penis is nearly normal in size, but changed in shape being flattened as a rule.

　　The corpora cavernosa are inadequately developed; the prepuce is triangular in shape, being diminished in its inferior half. Associated with this form of the deformity may be separation of the pubes, exstrophy of the bladder, atrophy of the testes, and cryptorchia.

2. *Penile Epispadias.*—In this variety the urethral groove traverses the entire length of the penis, but does not reach the neck of the bladder. The mucosa with which it is lined is red in color, but blends insensibly with the adjacent skin. The orifices of the various lacunae can be seen.

3. *Balanic Epispadias.*—This form is characterized by an abnormal opening on the dorsal surface of the penis at the base of the glans and the transformation of the balanic urethra into a gutter. On spreading out the parts, the bottom of the broad deep gutter is seen to connect with a median anterior-posterior slit which connects behind with the abnormal opening into the urethra.

This slit is limited on each side by two longitudinal crests which separate it into two lateral slits or grooves of smaller size. The crests are formed of the mucous membrane elevated by the corpora cavernosa. At the anterior extremity of the median groove the raphae is found to be attached much further forward than usual. The penis is short and thick, and the corpora cavernosa are completely united below, with no trace of an urethra between them.

II. *Epispadias in the Female Sex.*

This is extremely rare, and is characterized by absence of the anterior commissure of the vulva, and a fissure separating the prepuce and glans of the clitoris into halves. The urethra is open on its superior
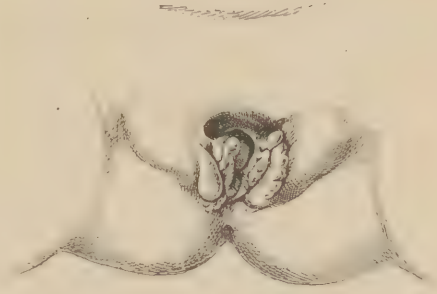
FIG. 34.—Epispadias in a little girl of 20 months. (*Redrawn from Kirmisson.*)

surface, and the mucosa of the bladder can be recognized by its deep violet color. The patients are annoyed by incontinence of urine, but the deformity does not prevent the sexual or reproductive functions from being fulfilled. A case observed by Nunez had become the mother of a child at 25 years of age. Cases of epispadias in the female have been reported by Kirmisson, Guyon, Mercier and others.

Kirmisson uses the symphysis pubis as the criterion for the differentiation of exstrophy of the bladder and epispadias. If there be no symphysis the case is one of exstrophy; if there be one, it is epispadias.

VI. In the Perineal Region

Imperforate Anus

Atresia ani, atresia recti, atresia ani et recti, and atresia ani et recti cum fistula vesicale, perineali, scrotali, vaginali sue suburethrali, are congenital malformations individually or collectively known as imperforate anus.

Their external manifestations vary; there may be no anal opening, there may be an anal opening that does not communicate with the rectum, there may be abnormal or fistulous openings connecting the rectum with the exterior or with neighboring viscera. The condition, therefore, includes external visible and internal invisible defects of development, a proper understanding of which is dependent upon knowledge of the manner in which the parts develop embryologically.

In the examination of the lesions already explained, it was pointed out that at the tail end of the young embryo, upon the ventral surface, there was an important structure known as the anal plug, with the anterior part of which we were busied in the explanation of the malformations of the inferior part of the abdominal wall, the bladder and the anterior part of the urethra. Present interest centers about its posterior part, the function of which is to excavate an opening into the rectum to constitute the anus. This takes place between the fourth and

fourteenth weeks of embryonal life. At the time at which the interest begins, the hind end of the embryo is conical and corresponds with the tail of the lower animals. Into it the primitive intestine descends almost to the tip, some distance beyond the position of the anal membrane, and the location of the future anus, in the form of a blind end that is known as the *post-anal gut*, and is destined to disappear by atrophy. What may result should any of it persist will be considered later.
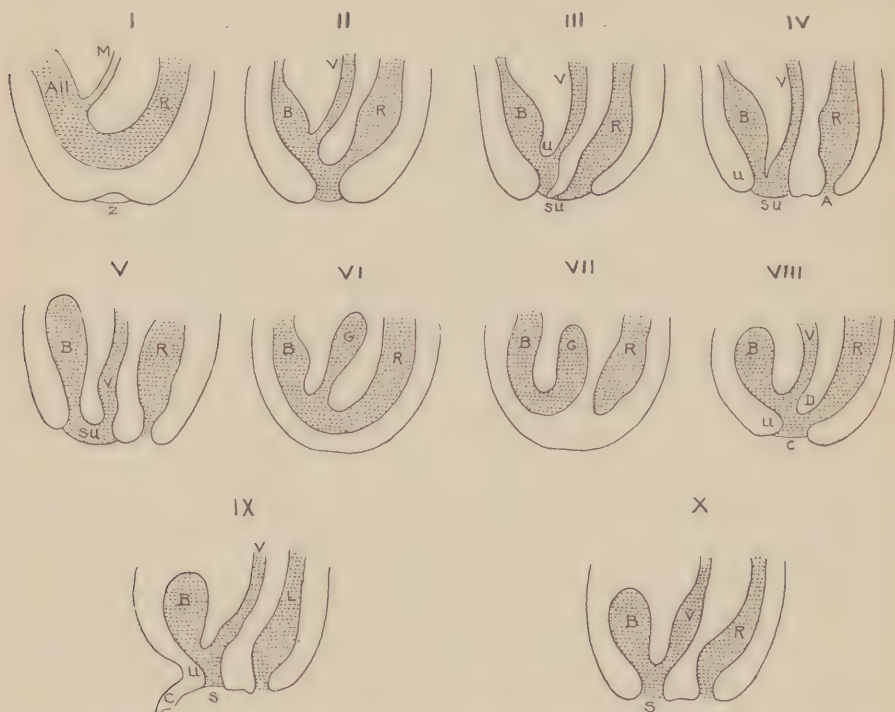
FIG. 35. —Schroder's diagram illustrating the embryological development, anatomical relations and malformations of the female cloaca and sinus-urogenitalis. I. The rectum (*R*) is continuous with the allantois (*All*), the future bladder, which receives the ducts of Müller (*M*), which form the future uterus and vagina. II. The depression (*z*) has deepened and effected a communication between the now forming bladder (*B*) and the rectum (*R*), the cloaca (*Cl*). III. The cloaca has divided through the downward growth of the perineal spur, separating the sinus uro-genitalis (*Su*) from the future anus (*A*). IV. The perineum has completely formed, separating the anus (*A*) from the opening of the sinus uro-genitalis (*Su*). The two ducts of Müller have united and the forming vagina (*V*), is separating from the future urethra (*U*). V. The upper part of the sinus uro-genitalis has narrowed to form the urethra, the vagina (*V*) is formed throughout its full length, and the sinus uro-genitalis (*Su*) has become the vestibule into which both open. VI. Complete atresia of the vulva. The rectum (*R*), the genital canal (*G*) and the bladder (*B*) all communicate. VII. Complete atresia of the vulva. The allantois has separated from the rectum (*R*). The bladder (*B*) and the genital canal (*G*) are distended with urine. VIII. Atresia of the vagina and anus. The perineum has not been formed, and the cloaca persists. The bladder (*B*), the vagina (*V*), the rectum (*R*) and the urethra (*U*) have a common outlet. IX. Hypospadias in the female. This degree is associated with hypertrophy of the clitoris (*C*), persistent sinus uro-genitalis (*S*) which forms a long canal into which open the urethra (*U*) and the vagina (*V*). X. Hypospadias of the more usual variety. The allantois is entirely transformed into the bladder (*B*) which is without an urethra, and opens directly into the uro-genital canal—*i.e.*, into the vestibule. Vagina (*V*); rectum (*R*).

The embryonic tail may be said to end at the point at which the allantois is given off, where there is usually a distinct expansion—a kind of blind cul-de-sac—bounded by the wall of the primitive gut, and anteriorly by the infundibuliform expansion of the beginning allantois above and the anal membrane below. At this time there is no separation of urinary and fecal

passages, and if at this time the anal plug was to open a passage from the exterior into the pouch, it would correspond to the cloacal passage of birds. But in the higher animals this does not occur, and before the opening is effected, the cloacal structures undergo a complicated series of developmental changes resulting in the formation of new organs. From the arch at the anterior part of the vault of the cloaca, a ridge descends upon each side, and soon assumes the appearance of a fold or curtain passing from the lateral wall towards the middle line—the membranes or folds of Rathke. Having reached the middle line, they concresce, beginning above, continuing downwards throughout their entire length, and separating the cloacal pouch into two divisions, the anterior of which is the sinus uro-genitalis, the posterior the rectum. It is easy to understand that any arrest of development in the progress of this concrescence must result in subsequent abnormal communication between the rectum and some part of the later developed urinary organs—*recto-vesical fistula*.

Though most of the modern embryologists accept the division of the cloaca by the folds of Rathke, some adhere to an older idea of how the separation was affected, and explain it through the development of a spur that Retterer conceived to descend from the anterior support of the intestine behind the pillar of the allantois. Tourneaux believed that the folds of Rathke were nothing but the pillars of this spur. But fortunately it makes no matter how the cloacal space is divided; it is the perfection or imperfection of the division that is important. If it is imperfect, some kind of fistula must result.

But the rectum thus separated from the cloaca, is still a blind pouch or, to be more correct, a blind tube, and would so remain were it not for the anal plug through whose dissolution an opening is effected into it. This opening is, however, curiously long postponed, and usually not effected until embryonic development is completed and the stage of fetal development reached.

The posterior part of the anal plug, as has been said, is alone concerned in the formation of the anus. Around it the mesoderm grows with the formation of a kind of cushion that extends forward towards the genital eminence and folds and constitutes the beginning of the perineum, and to furnish the material from which its aponeurotic, muscular and other structures will be formed. When it is fairly well developed, the position of the future anus can be seen in the form of a depression or excavated space still closed at the bottom—the external cloaca of various writers.

The actual opening of the anus results through the dissolution of the anal plug. Its cells become vacuolated, the vacuoles coalesce and eventually the whole mass of cells disappears. If the dissolution of the anal plug miscarries—i.e., is arrested—the anus remains closed, and atresia ani results. If the dissolution take place normally, but the rectum, at the time, is situated high up, the opening fails to communicate with it, and again atresia recti results. If in either case there have been preceding arrest of coalescence of the folds of Rathke, the atresia must be associated with an abnormal communication between the urinary and fecal passages.

Imperforate anus assumes many forms. Indeed Guersant is said to have operated upon 30 cases, no two of which were exactly alike. With a condition of such protean character it is easy to understand that classification is difficult.

Trelat divides the cases into four groups:

    1. Strictures.
    2. Imperforations.
    3. Absences.
    4. Abnormal Communications.

Le Dentu and Delbet follow this classification but also find it convenient to divide the cases clinically into those in which the expulsion of fecal matter is possible and those in which it is not.

A somewhat more elaborate classification was devised by von Esmarch, and was the foundation of that published, in 1892, by Rudolph Frank in his mono-

FIG. 36.—Diagram of the different forms of ano-rectal atresia. I. Atresia ani. *s*, Symphysis pubis; *B*, bladder; *R*, rectum; *x*, normal position of the anus, which is entirely absent, the perineal surface being smooth. II. Atresia ani et recti. *f*, A fibrous band passing from the more highly placed rectum, towards the perineum, which is again smooth, and without a sign of an anus. III. Atresia recti. Here the anus, *x*, is formed, but does not connect with the rectum except by means of a fibrous cord. IV. Atresia ani cum fistula vesicali. Again there is no anus or dimple in its place. V. Atresia ani cum fistula perineali, scrotali, et suburethrali. In such cases there may be no anal orifice, or a very small one. VI. Atresia ani cum fistula vestibulari (vulvari). (*Rottner.*)

graph, as well as that used by Stiede in his paper in Langenbeck's Archives in 1893. It is also adopted by Forgue in his "Precis," and seems to leave little to be desired.

    I. *Atresia of the Anus or Rectum without Complications.*
        1. Simple Atresia of the Anus. In this form the rectum terminates blindly in the anal region as there is no anus, and usually no depression where it should be.
        2. Simple Atresia of the Rectum. In these cases there is a well-formed anus, but it opens into a short blind passage that ascends toward the rectum.
        3. Ano-rectal Atresia. In these cases there is a considerable interval between the blind termination of the rectum and the imperforate anus.
    II. *Ano-rectal Atresia Complicated by Internal Communications.*
        1. In Females,
            (*a*) Between the rectum and the vagina.
        2. In Males,
            (*a*) Between the rectum and the bladder.
            (*b*) Between the rectum and the urethra.
            All of these communications are the result of arrested development of the membranous separation of the cloaca into the rectum and sinus uro-genitalis. They are essentially different from those of the next group which are attributable to later developing pathological conditions.
    III. *Ano-rectal Atresia Complicated by External or Pathological Communications or Fistulae.*
        1. In Males,
            (*a*) With perineal fistulae in the middle line.
            (*b*) With scrotal fistulae.
            (*c*) With sub-urethral fistulae.
        2. In Females,
            With vestibular fistulae opening into the vulva.

With so many variations it is inevitable that the appearance of the affected region shall vary considerably in different cases. In some there is nothing to mark the normal position of the anus but a dimple with radiating wrinkles; in others it is marked by a tissue thickening suggesting a cicatrix; in still others there is a delicate membranous structure that closes a fairly well formed anus, and through which it may be possible to see the meconium in the rectum beyond.

In cases of rectal atresia, the general aspect of the external parts may be quite normal, and it is only when the finger is introduced into the anus and fails to find its way into the rectum that the true nature of the disturbance is recognized. The anal opening, though appearing normal to the eye, may be so small that only a probe can be introduced into it and find its blind end. In most cases the presence of a well-developed rectum beyond can be counted upon, but a few are known in which the rectum was represented only by a slender canal or even a solid fibrous cord.

In still more rare cases the position of the external anus is entirely unmarked, and the surface between the buttocks smooth. In such cases the malformation ought to be detected at once; in those in which there is an anus covered by a membrane through which the contents of the rectum can be seen it ought to be detected soon through inspection of the parts; in cases in which there is an external opening large enough to admit the finger tip examination may not be made for several days because the parts seem normal.

The unrelieved condition is incompatible with life, unless there are associated communicating passages through which the contents of the bowel may be evacuated. Even with such passages, however, the evacuations may be possible only so long as the contents of the bowel are fluid. So soon as the feces are formed there is complete obstruction. But a very large fistula may suffice for all time, and Morgagni speaks of a woman who lived a hundred years, always having the bowels move through the vagina because of an imperforate anus.

A peculiar and interesting group of cases called "Imperforation through multiple segmentation" by Le Dentu and Delbet, are characterized by several communicating passageways between the anus and the rectum. Cases of this form of imperforation have also been seen by Veillemin, Lannelongue, Marchand and others.
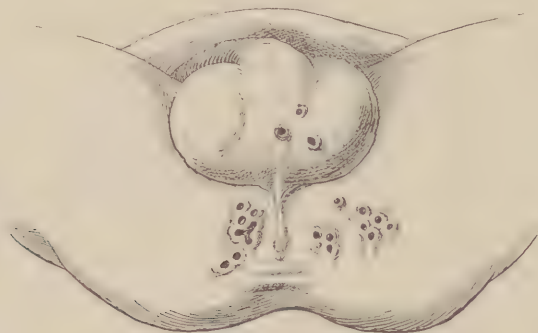
Fig. 37.—Multiple ano-rectal and perineal openings in a case of atresia ani. (*Redrawn from Kermisson.*)

Another interesting modification, the precise etiology of which is uncertain, is imperforation accompanied by multiple perineal fistulae. Kirmisson has called these "ectopias of the anus" and in one of his cases there were no less than 20 of these perineal openings, each surrounded by a small annular elevation suggesting an anus in miniature. Strictly speaking these were not confined to the perineum, but were distributed over it, the scrotum and the inter-gluteal folds.

Rare external fistulae, i.e., integumentary openings in unusual positions have been reported. If incompatible with the facts of embryology, they must be referred to subsequent pathological conditions. Thus, Mery has reported a case in which the fistulous opening was at the umbilicus, and Fristo one in which it appeared above the sacrum, having traversed the body of the fifth lumbar vertebra.

Of the internal fistulous passages the most frequent connect the rectum and the bladder or urethra. In 1905 Grisel published a collection of 84 cases, in 31 of which the fistulas led into the bladder near the trigone, and in 53 into the urethra, either its prostatic or bulbar portions. In some of the cases the passages were of good size, but most of them were very narrow.

In females the fistulas almost always open into the vagina. There is however, some question as to the exact anatomical position of the external opening.

It is said most frequently to occur just below the hymen in the immediate vicinity of the posterior fourchette. Some seem to regard this as vaginal, some as vulvar, some as perineal. Reported cases of urethral fistulas in females must be regarded with suspicion of error. Some writers seem to doubt the propriety of including cases of stenosis with those of atresia, but if it be remembered that the variations pass through all intermediate stages between wide blind

FIG. 38.—Malformation of the anus. Enterodenum (hindgut) continued as a tapering, tortuous tube (a) along the raphe of the scrotum, and ending by a minute opening (b) discharging meconium near the end of the penis; c, anal depression—imperforate. (*Peters.*)

passages into which the finger can be passed to narrow ones only to be traversed by a probe, and finally to those in which the anal and rectal tissues are connected by a fibrous cord, it seems perfectly justifiable to do so. The only essential difference between the two is that in atresia the passage is entirely closed, and in stenosis it is almost closed. Curiously enough the cases in which the rectum and anus were said to be connected by a fibrous cord with a very narrow passage appear almost entirely in the older literature. Scultitis is said to have seen a new-born infant whose anus scarcely admitted the point of a pin; Ronnhuysen a little girl whose anus was so stenosed as to permit the passage of only liquid feces.

The reported cases may be divided into groups according to the form of constriction as follows:

1. *Stenosis Depending upon Annular Constriction.*
   In these rare cases the anus and rectum are connected by a slender tube lined with mucous membrane, evidently a malformed rectum.

2. *Stenosis Depending upon the Presence of Membranous Diaphragms.*

Such cases have been studied by Reynier, who found them to vary. In some cases the membranous diaphragms are thin and delicate, in others thick and tough. They may surround the rectal tube in annular form, only partly surround it, or form obstructing spurs. Annular formations may have a very narrow lumen.

3. *Stenosis Depending upon the Presence of Transverse Bands.*

Such were first pointed out by Tillaux in 1895. The stenosis depends upon the presence of more or less prominent transverse bands, situated in the rectum a few centimetres above the anus. They are apt to be associated with dilatation above and fistulation below.

The frequency of ano-rectal malformations is given by Trelat as 1:11,000, by Collins as 1:16,000. They are apt to be hereditary like other arrests of development, and Hadra observed one family in which there were six cases.

Hypospadias

Hypospadias is a congenital malformation characterized by the presence of a median fissure in the inferior wall of the urethra.

It is more frequent than epispadias, and is almost entirely confined to the male sex, only two or three cases have been seen in females.

It is customary to arrange the cases in three groups according to the appearances presented. Beginning with the most complex deformities and passing to the most simple, they are:

I. *Perineo-scrotal Hypospadias.*

These cases give rise to the greater number of male pseudo-hermaphrodites, some of whom live throughout their whole lives under the misapprehension that they are
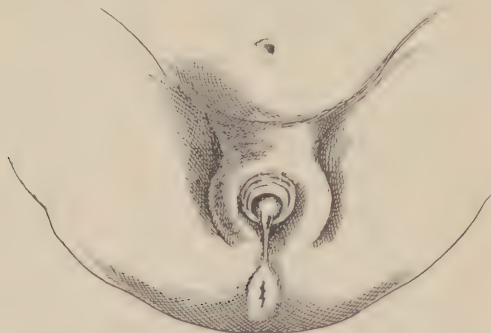
FIG. 39.—Perineo-scrotal hypospadias in a little boy of 15 days. (*Redrawn from Kirmisson.*)

women. And, indeed, the mistake is natural for the configuration of the sexual organs is much more like those of the female than those of the male. The penis is very short and slender, and is not perforated by an urethral canal, so as easily to be mistaken for a clitoris. The scrotum is divided, the halves remaining separated from one another by a vertical slit much resembling a vulva. The testes may be ectopic, i.e., have remained in the abdominal cavity, hence the halves of the scrotum resemble the labia majora. If they have descended, they may be small and atrophic, and scarcely palpable in the halves of the divided scrotum. To determine the sex it may be necessary to make a rectal examination to discover the presence or absence of uterus and ovaries. The urethral orifice is in the angle formed by the scrotum and perineum.

II. *Peno-scrotal Hypospadias.*

This is a rare form characterized by an opening, into the urethra somewhere along its inferior wall between the glans and the scrotum. It takes the form of a linear slit along the under surface of the penis, at the bottom of which the mucous membrane of the urethra is seen. The length of the defect varies, sometimes including the greater part of the penile portion of the passage, sometimes being very short and resembling a fistula resulting from accident. Usually there is only one defect,

Fig. 40.—Peno-scrotal hypospadias in a little boy of 5 years. (*Redrawn from Kirmisson.*)

sometimes there are two. One of them may be in the penile, the other in the balanic portion of the urethra. The urethra beyond the opening may be normal and patulous, or may terminate in a cul-de-sac.

If the opening into the urethra gap, or be made to gap by separating its edges, the urethra itself appears as a shallow gutter when the penis is flaccid, as a deep one when it is erect. The mucous membrane at its edges is continuous with the skin. When an attempt is made to close the defect it is found that it is not a mere separation of the tissues by which the defect is brought about, but actual absence of the tissue of the posterior part of the canal. In some cases most of the urethral tissue is absent, and only represented by a kind of fibrous cord, whose contraction seems to be the cause of the not infrequent peculiar curve and twist of the penis. Associated deformity of the penis from arrested development of the corpora cavernosa is frequent.

III. *Balanic Hypospadias.*

In this variety the defect is entirely confined to the neighborhood of the glans. The urethra does not open, as normally, at the meatus urinarius, but at the base of the glans, in an orifice that is variable, but always associated with deformity of the glans itself. The deformity centers about the meatus which it modifies in various ways. Thus their may be:

    1. A meatus with four lips.

    2. A double or binocular meatus.

    3. Double meatus with four lips.

According to Kirmisson the deformities incidental to balanic hypospadias may chiefly affect the glans, the urethral structure of the glans, or the prepuce.

    (*a*) Urethral malformations.

        1. In front of the abnormal opening into the urethra, there is a gutter of variable depth, that represents the position of the urethra, and continues forward to where the normal meatus should be.

        2. In front of the abnormal opening there may be a normal meatus opening into a tubular cul-de-sac.

    (*b*) Glandular malformations.
        1. The glans may be flattened and show downward curvature.
        2. There may be no frenum.
    (*c*) Preputial malformations.
        1. There may be no inferior portion.
        2. There may be increase and thickening of the superior part, which covers the corresponding part of the glans, like the cap of the prepuce, but does not pass beyond it.

The entire penis is apt to be malformed, and is commonly twisted. Verneuil has reported a case in which the dorsal surface of the penis was in relation with the scrotum, the urethral surface being directed forward and to the left. Sometimes the penis is recurved downward.

Hypospadias in females presents entirely different appearances because the urethra naturally opens in the vestibule, and does not pass through the clitoris. The only possible form, therefore, is the homologue of the perineo-scrotal form. Krajewski operated upon a girl aged 17 years, whose urethra was without an inferior wall for a distance of one and a half centimetres. The normal part did not measure more than one-half centimetre in length and the general appearance was that of a gutter in the superior vaginal wall. The patient had complete incontenence of urine.

Kirmission examined a little girl three months of age, and found a somewhat similar condition: "there were, at the level of the vulvar region, two little orifices, one situated below the region of the clitoris, where the normal meatus ought to be, the other a little below, and directed towards the vaginal orifice. The two were separated by a membranous bridge about a centimetre in length. A probe introduced into the former, came out of the latter. When the membranous bridge was cut, the urethral mucosa appeared."

All forms of hypospadias are arrests of development, and easily accounted for embryologically.

In explaining the origin of the ano-rectal malformations it was shown that the cloaca became divided into the rectum and uro-genital sinus after which attention was directed solely to the former; it now becomes necessary to more particularly consider the latter, as from it the bladder and a portion of the urethra develop.

With the uro-genital sinus certain important tubular structures connect, and into it they may be said to empty. To them it will be necessary to return again later in other connections; at present it is sufficient to know, that they are the Wolffian ducts, the Müllerian ducts and metanephric ducts. The former two of these undergo extensive modifications if they are to persist in later life, the latter progressively enlarge to become the ureters.

The changes that take place in the further development of the uro-genital sinus and the structures arising from it differ according to the sex of the embryo. If it be a male, the metanephric ducts ascend to form the ureters, the Wolffian ducts descend to form the seminiferous ducts, and the Müllerian ducts practically disappear. The uro-genital sinus eventually becomes expanded in its central part to form the bladder, its extreme upper part becomes reduced to a mere fibrous cord, the urachus, or disappears altogether, and its most inferior part remaining narrow and tubular becomes the urethra.

If it be a female, the metanephric ducts behave similarly, and become the ureters, the Wolffian ducts practically disappear, and the Müllerian ducts greatly increase in size and importance, uniting to form the genital tube, and evolve into the uterus and vagina.

In both sexes the urethra, with which hypospadias is chiefly concerned, begins as a tubular inferior termination of the uro-genital sinus, but continues as a canal, short in the female, and long in the male, whose formation is entirely different in the different sexes.

To understand it it is necessary to review the development of the external sexual organs which form, so to speak, about the urethral canal.

At about the fifth week, and shortly before the opening into the uro-genital sinus has been effected by the anterior portion of the anal plug, the mesenchyme of the anterior inferior part of the ventral wall, heaps up so as to form an eminence, the genital tubercle, which somewhat rapidly increases in size, and soon becomes bulbously expanded at its extremity, and marked by a groove which extends from the tip to the base separating two ridges which become the genital folds. At about the tenth week, the mesenchyme on each side of the genital tubercle forms a swelling—the genital swelling—and the indifferent sexual stage of the embryo is reached. At this time it is impossible to tell by an examination of the exterior whether the embryo will become male or female. All that can be seen is a central prominence that will become the penis in the male, or the clitoris in the female, with a deep groove on the under side, that will become the urethra of the male, and a swelling on each side that will become the halves of the scrotum in the male, or the labia majora of the female.

If the embryo develop into a male, the genital tubercle greatly enlarges and elongates to form the penis, and soon becomes encircled by a slight constriction, not far from the free end, that serves to mark the point at which the body is separated from the glans. By the twelfth week the knob-like extremity has become well marked and surrounded by a tegumentary fold that gradually advances over it to form the prepuce which at first is adherent to the subjacent structures. The bulk of this rudimentary structure will become the future corpora cavernosa, but the part beyond the constriction will become the glans. As development proceeds, the groove on the under surface deepens and then slowly becomes obliterated beginning behind at the urogenital sinus and continuing forward to the glans, thus closing in a canal that is in reality a continuation of the lower narrow part of the uro-genital sinus. The genital ridges, increase in size rather rapidly towards the close of the fourth month, and eventuate in two pouches which coalesce in the middle line to form the scrotum, the line of union remaining visible as the raphae. Almost the last stage in the perfection of the external genitalia is the separation of the prepuce from the glans to which it has all along been adherent, through keratinization of the lower layers of its epiderm.

If the embryo develop into a female, the other parts outgrow the genital tubercle which remains small and becomes the clitoris, and the genital folds which also remain small and form the labia minora or nymphae. The genital swellings grow large, but do not coalesce, and become the labia majora, one on each side of the genital outlet. The urethra, which is especially concerned in hypospadias, in this case has no connection with the external genitalia, but is concerned with the further development of the deeper parts. Is there any difference in the source of the urethral tissues of the female, or does it like that of the male descend from the inferior end of the uro-genital sinus? Probably, but the development of these parts in the female is complicated. As worked out by Retterer, after the sinus uro-genitalis has been separated from the rectum by the concrescence of the folds of Rathke, there is a second partitioning, through the development of other spurs and folds, which form between the neck of the future bladder and the insertion of the Müllerian tube, by which the lower part of the sinus becomes divided into the tubular segments, one of which becomes the lower part of the urethra, the other the lower part of the vagina. Here, however, it becomes confused with the greater part of the vagina which is formed from the modified Müller's tubes. According to Retterer the upper part of the vagina is in relation with the base of the bladder and the upper part of the urethra that is derived from the Müller's tubes, while the lower portion of the posterior wall where the sphincter is interrupted is derived from the uro-genital sinus.

In addition to the embryological theory of hypospadias, it is necessary to mention the pathological theory. No one now accepts it, but Haller, Dionis, and later Kauffman continued to support it as late as 1886, referring the malfor-

mation to rupture of the urethral canal during fetal life in consequence of obstruction of the urethra and retention of urine.

Before dismissing the subject it may be well to mention that *congential stenosis or atresia of the urethra* is sometimes observed. It seems to result from defective development of the balanic portion of the urethra, by which the meatus urinarius is too small to permit the ready outflow of the urine. In a few cases it seems to depend upon congenital small size of the opening of the prepuce.

VII. In the Reproductive Organs

Cryptorchia; Ectopia Testis; Undescended Testicle

Physical examination of the scrotum of young infants frequently results in the discovery that there are no testes. If the children are but a few months old, this has little significance as it is common, for children to be born with the testes still in the act of completing their peculiar migration or "descent." If however, they are already several months old, and one or both testes are missing, a careful examination should be made to see if they can be found at some part of their course. Further, if the parent or nurse call attention to a swelling in the inguinal region of a young child, or if one be found in the perineal region, it is important to exclude the possibility of its being a testis before it is assumed to be something else, and some treatment adopted that may prove injurious in the light of future events. Thus, it has not infrequently been found, some time afterwards, that what was at first supposed to be an inguinal hernia was in reality an undescended testis, whose progress was completely and irremediably prevented through the application of a truss.

Not infrequently cases of undescended testes remain undetected until puberty, either because no examination was made, or because it was assumed that being absent from the scrotum there were none. With the sexual development at puberty, the organs enlarge, and, if ectopic, suffer from compression in their abnormal environment, with the occurrence of pain of a neuralgic character, and occasional paroxysms of great severity associated with vomiting, prostration, small weak pulse, anxious expression, and chills. This may be but the beginning of a more constant pain arising from inflammation of the testis, that may eventually extend to the peritoneum. Such cases should be operated upon in time to prevent these accidents, not with the intention or expectation of successfully replacing the testis in its proper position, which has never entirely succeeded, but for the purpose of removing the offending organ which sooner or later becomes useless in its abnormal environment, as the result of pressure atrophy. In a considerable number of cases of unilateral ectopia operated upon by Biegel, no spermatozoa were found in the seminal fluid. Follin found the same thing, and attributed it to fibrous and fatty degeneration of the ectopic organs. Godard supposed their absence to result from the anemic condition of the ectopic organs. Monod found spermatozoa in the ectopic testes of a man of 20 years, but none in those removed from two men of 40 years. The matter was carefully studied by Bezancon who came to the conclusion that "it is only

occasionally that one finds atrophy of the inguinal testes of children and young men."

Upon dissection it is usually apparent that the testis, cord and epididymis are simultaneously ectopic, maintaining their normal relationships to one another. But sometimes the testis becomes fixed in the abnormal position while the cord, epididymis and vas deferens continue their descent to the bottom of the scrotum. In very rare cases the testis has been found divided, a part of it remaining in the ectopic position, the remainder continuing its descent, and resulting in a peculiar elongate and malformed structure consisting of the two separated segments of the testis, the epididymis, and the connecting vas.

Ectopia testis is frequently associated with hernia, of which more later.

If a testis is not in the scrotum, the chances are against its having remained in the abdominal cavity, for that is very rare. Search ought to be made for it, and the chances are that it will be found either in the crural or perineal region.

In the former case—*crural ectopia*—the organ, having escaped from the inguinal canal, or having in some way passed through its anterior wall becomes driven back towards the root of the thigh, in a position corresponding to that of the crural or femoral hernia. In the latter—*perineal ectopia*—it is driven backward upon the perineum, a little to one side, and a short distance in front of the anus, where it usually lies superficially and can easily be moved beneath the skin. Perineal ectopia is rare, but Terrillon collected 30 cases, and Kirmisson and Curling each saw one. Kermisson's case was bilateral, both testes lying beneath the skin of the perineum.

It might be supposed that the explanation of ectopia testis on embryological grounds would be easy, but it soon involves a number of difficult questions, some of which are, at present, unanswerable.

Neglecting, for the time being, the origin of the testis, and considering only its movement from the position, high in the abdominal cavity where it is first formed, the progress of events is divided, by McMurrich into three stages as follows:

1. The first stage, which eventually brings about the second, and depends upon the slow rate of elongation of the inguinal ligaments or gubernacula testorum, is very slow until after the fifth month.

2. The second stage finds the testes in the inguinal portion of the abdomen, from which they ascend slightly, for a short time.

3. The third stage is that of final descent, during which the testes pass out of the abdominal cavity and take up their position in the scrotum. It begins by the prolongation of the vaginal processes of the peritoneum and their extension downward into the scrotum. As the gubernaculum testis is attached to the bottom of the vaginal process, and since its growth has greatly diminished, the testes are again gradually drawn downward to the infundibular region and into the scrotum, slipping between the vaginal process and the infundibuliform fascia, which together with the other layers of the scrotal wall are differentiated about this time. The condition thus developed persists for some time after birth, the testis being readily pushed upward into the abdominal cavity along the same path by which it had descended. Later, however, the size of the openings in the vaginal process become greatly diminished, and each converted into an upper narrow neck and lower sac-like cavity, while still later the walls of the neck portion fuse and become converted into a solid cord, while the lower

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portion wraps itself around the testis to become its tunica vaginalis. Through these changes the testes become permanently located in the scrotum. During the descent of the testes the remains of each Wolffian body, the epididymis and the upper part of each vas deferens, together with the spermatic vessels and nerves, are drawn down into the scrotum, and the mesenteric fold in which they were originally contained also practically disappears, becoming converted into a sheath of connective tissue which incloses the vas deferens and the vessels and nerves and binds them together into what is termed the spermatic cord. The mesorchium which united the testes to the peritoneum enclosing the Wolffian body, does not share in the degeneration of the latter, but persists as a fold extending between the epididymis and the testis and forming the sinus epididymis.

McMurrich also appends the statement that in most books of anatomy the spermatic cord is described as lying in the inguinal canal, which traverses the abdominal walls obliquely immediately above Poupart's ligament.

So long as the lumen of the neck of the vaginal process of peritoneum remains patent there is a canal placing the cavity of the tunica vaginalis testis in communication with the general peritoneal cavity, but the cord does not traverse this canal, but lies outside of it in the retroperitoneal connective tissue. When however, the neck of the vaginal process disappears, a canal no longer exists, although the connective tissue which surrounds the spermatic cord and unites it to the tissues of the abdominal wall is less dense than the neighboring tissues so that the cord may readily be separated from them and so appear to lie in a canal.

The term *ectopia testis* signifies no more than congenital malposition of the testis. Practically all known cases result from failure of the organ to successfully complete its regular descent. It is the result of arrest of development, and as usual, there are few cases in which the arrest occurs very early so that the testis remain high up in the abdominal cavity, and many in which it occurs late and is detained in the inguinal canal. The condition may be unilateral or bilateral; the latter are comparatively very rare. Kirmisson groups the cases thus:

1. The testis rests at some point in its descent:
    (a) In the lumbar region.
    (b) In the iliac region.
    (c) In the inguinal region.
2. The testis lies under the skin:
    (a) Of the abdominal wall.
    (b) Of the root of the thigh.
    (c) Of the perineum.

(a) *Lumbar or Sub-renal ectopia* is very rare. The testes or testis remain in the abdominal cavity, at about the same point at which it was originally formed.

(b) *Iliac ectopia* is also rare, but Godard found it seven times out of fifty-eight cases of unilateral ectopia. It represents a more advanced step in the descent, the testis having reached the iliac fossa, immediately behind the orifice of the inguinal canal.

(c) *Inguinal ectopia* is by far the most frequent variety, and was found by Godard to comprise thirty-nine of his fifty-eight cases or a total of sixty per cent. It includes cases in which,
    (a) The testis has been arrested in the inguinal canal.
    (b) The testis has passed through the canal.

In these different positions the testis is usually free, but may be fixed by adhesions. The relation to the peritoneum is variable. The testis may be in the general peritoneal cavity, but in occasional cases has its own peritoneal envelope. As the peritoneum precedes the testis into the scrotum, the ectopia may be followed by descent of the intestine; hence the frequent association of ectopia and hernia. The infra-abdominal ectopia of some writers seems to be but a variety of inguinal ectopia.

(d) *Cruro-scrotal ectopia* is a term used by Godard for a variety in which the testis passes through the inguinal canal, but is arrested at the root of the scrotum, or at the fold that separates the thigh from the scrotum. In this position it is surrounded by a serous prolongation that continues into the inguinal canal. It is a very rare condition.

(e) *Crural ectopia*, also a very rare variety, is said to parallel ectopia of the ovary, though its mechanism is different. It is supposed to depend upon the fact that the testis, having escaped through the anterior wall of the inguinal canal is driven back toward the root of the thigh to the usual position of the crural or femoral hernia.

(f) *Perineal ectopia*, is also rare, but Terrillon was able to collect 30 cases from the literature. In the only case observed by Kirmisson the testis was situated upon the right side of the perineum. Curling observed a bilateral case.

Ectopia testis is distinctly heritable, in which it resembles the greater number of arrests of development, and gives support to the theory that such conditions result from exhaustion of the developmental energy.

Gosselin followed the condition through three generations of the same family. Follin and Goubaux have shown that it is distinctly heritable in the lower animals. It is frequent among idiots, degenerates and epileptics.

The controversial aspects of ectopia testis center about the mechanism of descent, and the nature of its interruption. Since the writings of Godard, the chief factor has been pretty generally acknowledged to be the gubernaculum testis. If it be absent, the testis remains in the abdominal cavity. If its external faciculus, which inserts into Poupart's ligament, and directs the gland through the inguinal canal, alone exist, the testis enters the canal but goes no further, and inguinal ectopia results. If the middle faciculus, which normally is inserted in the bottom of the scrotum, and conducts the testis there, terminates in the skin, either in the cruro-scrotal fold, or in the perineum, a crural or perineal ectopia will result. Forgue, however, points out that "this motive specialization of the various fasciculi of the gubernaculum is only imaginary; the contractile power theoretically attributed to the two fasciculi of the gubernaculum, exceeds their anatomical value; it is further a physiological paradox since the two fasciculi, external and pubic, have exhausted their role, when the organ is found to have been brought to the altitude of their inferior insertion, precisely at the entrance of the inguinal canal through which it must pass." He believes, therefore that the idea of an active migration of the testis brought about through the contraction of a guiding muscular apparatus must be abandoned. In this he agrees with Kirmisson that "there is more imagination than reality about its importance. It is only occasionally that an abnormal attachment of the gubernaculum can be established." Godard however, observed a case of cruro-scrotal ectopia in which a slight strip of gubernaculum was inserted a little below the root of the penis, instead of at the bottom of the scrotum, and Jalaguier in operating upon a case of perineal ectopia, found that the testis was retained in its abnormal position by a strip of the gubernaculum inserted in the tuberosity of the ischium. In a good many cases the testis is found to be anchored to its abnormal position by peritoneal adhesions of prenatal origin. It is almost the rule for surgeons to find that not only the gubernaculum testis is shortened, but that all of the elements entering into the composition of the cord are similarly shortened.

In his general summary of the subject, Forgue expresses his ideas thus: Let us take the testis in its lumbar position: from its inferior pole to the inguinal region, there extends a fold of peritoneum with smooth muscle fibres. This is the "inguinal ligament" of Kölliker, or the "gubernaculum" of Hunter. At the level of the abdominal orifice of the inguinal canal, the inferior extremity of this gubernacular ligament prolongs itself into a long dense cellular cord, well studied by Soulie, which occupies the entire length of the future inguinal canal, leaving it at the external inguinal orifice by passing through the aponeurosis of the great oblique, perforated in the beginning, and losing itself in the mucous tissue that lines the interior of the scrotum. It is precisely this cellular cord that is the agent in the descent of the testis, drawing it down by progressive retraction, toward the bottom of the scrotal sac. Through the shortening that thus results, the inguinal ligament, and with it the peritoneum that adheres to its base and is to form the peritoneo-vaginal canal, as well as the testis, to the inferior pole of which it is attached, are drawn down. . . If the length of the gubernaculum (from the inferior pole of the testis to the internal orifice) is shorter than the distance which separates this orifice from the bottom of the scrotum (length which corresponds to the disappearing cellular cord) the testis drawn down by the gubernaculum, penetrates into the inguinal canal, and descends into the scrotum. But if the first length be greater than the second, the peritoneo-vaginal canal, forms completely or in part before the testis has been depressed below the external inguinal orifice, and has not accomplished its complete descent into the scrotum.

Both Forgue and Kirmisson point out that the testis may meet with obstacles that may impede its future progress.

Ectopia testis is frequently associated with congenital hydrocele and congenital hernia which will be considered later. At this point will be briefly mentioned complications of a different kind.

1. *Strangulation.*—This rare complication may occur when an ectopic testis is suddenly made to change its position. Thus, having appeared at the external inguinal canal, and been mistaken for a hernia, it is suddenly and violently forced upward into the abdominal cavity, where it is held by a truss; or, through the mistaken application of the truss is forcibly pushed down toward the scrotum. In either case the vessels are liable to compression, and symptoms similar to those of strangulated hernia brought about. The vague and neuralgic pains from which the patient may have previously suffered suddenly give place to violent pain in and radiating from the inguinal region, vomiting, at first of food, then bilious, finally fecal, with small pulse, prostration, cold sweat, and distension of the belly. Now in such cases it is not always possible to determine whether it is through the displacement of the testis that the symptoms are brought about, or whether they depend upon associated hernia. Such cases should always be operated upon, and the testis removed if it be at fault, or the hernia relieved, if present.

2. *Torsion of the Spermatic Cord.*—This possibility seems to have been first pointed out by Nicoladoni, who in 1883 operated upon a young man who had suffered from inguinal ectopia since the age of twelve years, and for three years had had a painful swelling in the groin. He found the testis thin, deformed, blue-black in color, and suspended from a pedicle formed by the two bundles of the cord with which it formed an arc of 180 degrees. The veins were full of coagulated blood, with hemorrhages in the rete testis, under the albuginia, and in the head of the epididymis. Kocher conceives

that a horizontal position of the testis is a predisposing cause of torsion, the spermatic vessels being more widely separated from the vas deferens than normal and leaving the testis free to turn upon itself.

3. *Cancer.*—The abnormal conditions that obtain in ectopia are supposed by many to to predispose the testis to cancer. Whether this is so or not cannot be scientifically stated. Monod and Terrillon, however, were able to collect 42 cases of malignant tumors that had their beginnings in undescended testes. A remarkable thing about them was that they occurred chiefly in young individuals. In 33 cases whose ages are given, 23 had not passed the 40th year, and 14 of them were between 30 and 40. Kocher saw a case of malignant disease of the testis in a child of seven years.

Both carcinoma and sarcoma have been reported.

Turning from the rare complications to the frequent ones, the first to be considered is:

Congenital Hydrocele

As the testis advances through the inguinal canal into the scrotum, it is preceded by a prolongation of peritoneum, which can with advantage be theoretically divided into three portions, an upper that lines the inguinal canal itself, a middle that surrounds the cord, and a lower, that surrounds the testis. These are respectively known as the inguinal, the funicular, and the vaginal portions. When the descent of the testis has been completed, the vaginal process remains to form the tunica vaginalis testis, and the other two disappear by constriction and atrophy. But should any arrest of development interfere with their disappearance, abnormalities present themselves either at once or at some subsequent time, according to the local conditions. Thus, the entire canal may remain open, when the intestine may prolapse and bring about congenital inguinal hernia; or, the inguinal portion may close, leaving the funicular and vaginal portions open, though separated from the vaginal portion; or, the vaginal portion may assume its normal size and development, while the inguinal and funicular portions are reduced to a very narrow canal through which it is scarcely possible to pass a fine probe; or, the inguinal and funicular portions may be reduced to a fibrous cord without any permeable canal.

In the event of the inguinal and funicular portions being reduced to a fibrous cord, no subsequent abnormalities are to be expected. But if they are reduced to a slender canal, a more or less permanent communication between the abdominal cavity and the cavity of the tunica vaginalis testis is established, and it is possible for fluid from the former to collect in the latter. Or, if for any reason the fluid should collect in the latter, to find its way into the former.

If the funicular process remains open, and the inguinal and vaginal processes close, fluid subsequently collecting in it would form a cyst in relation with the spermatic cord. If the inguinal portion remain open at the center, but close above and below, so as no longer to connect either with the abdominal cavity or that of the tunica vaginalis testis, it would be possible, through collection of fluid in its interior to have a cyst occur in the inguinal region. If the inguinal process disappears, and the funicular and vaginal processes remain open and in connection, any collection of fluid in their cavities, would extend high up into the neck of the scrotum and be in relation with both the testis and cord. Such, then are the possibilities, and the fluid collections referred to constitute the various forms of congenital hydrocele.

But thus far only the position of the fluid collections has been considered, and nothing has been said about their cause. That is indeed another and different matter, not thoroughly understood. All that can be said is that mild inflammatory disturbance is supposed to be the chief factor.

Cases may be divided into the following groups:

1. *Hydrocele from Persistence of the Vagino-peritoneal Canal.*—These usually do not appear until some time, often not for some years, after birth, and are characterized by their reducibility. The fluid can either enter or escape, the freedom of movement being
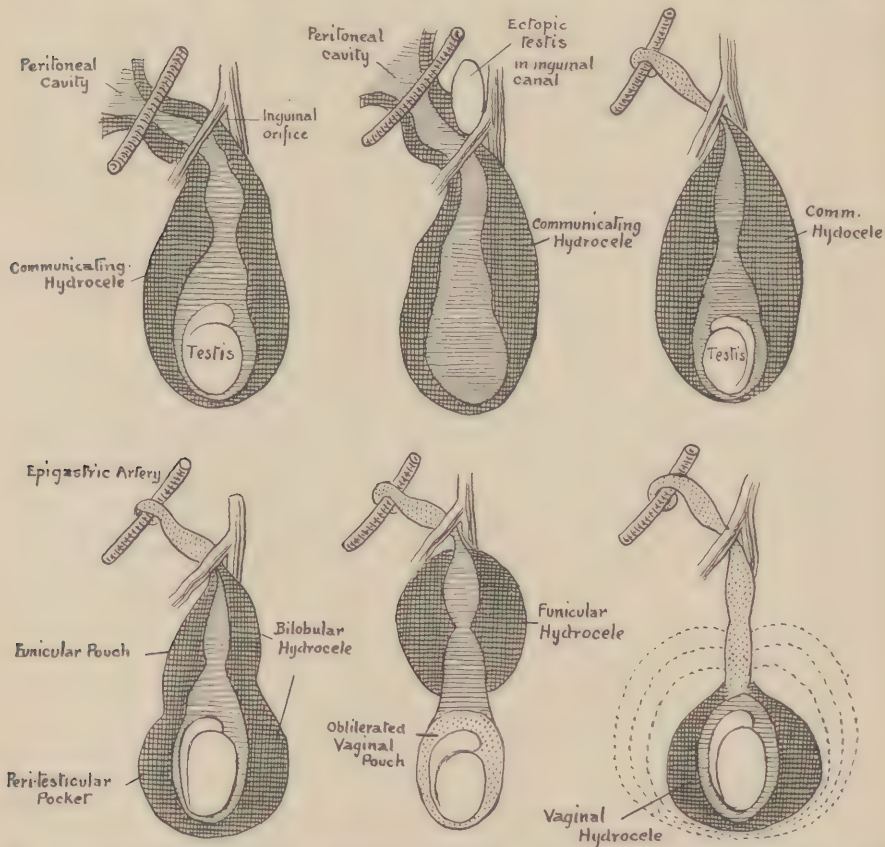
FIG. 41.—Diagram showing the different varieties of congenital hydrocele. (*Redrawn from Forgue.*)

in proportion to the size of the communicating passage. In rare cases the testis is said to act as a kind of ball valve, preventing the free movement of the fluid when the sac is compressed. Kirmisson thinks that more is to be learned by questioning the patient than by physical examination. If the fluid collection is larger in the evening than in the morning, it indicates that it collects slowly during the daytime, and flows out at night. Otherwise the conditions are like those of other hydroceles. That is, they form scrotal tumors of translucent fluctuating quality. Even with free communication between the abdominal cavity and tunica vaginalis testis, it is unusual to see hydrocele in healthy children, but in those that were sickly, emaciated and especially in the tuberculous Kirmisson found that the scrotum soon filled up. He interprets this to mean that the occurrence of the hydrocele is not due solely to the mechanical disturbance.

Out of 124 hydroceles examined, Bryant found that only five (4%) communicated with the abdominal cavity. Melchiori, however, found it in 27 out of 282 cases (7%). He observed bilateral hydroceles of this kind 4 times out of 21 cases. It is very rare to find hernia and hydrocele of this kind coexisting, supposedly because when the communicating passage is large enough to permit the intestine to enter, it readily permits the fluid to flow out. Such congenital hydroceles undoubtedly tend to spontaneous cure, which may be no more than final, though delayed perfect development.

2. *Infantile Hydrocele.*—These seem to have no embryological significance or developmental importance, but are to be referred to accidents occurring at the time of birth, or to subsequent disease. They are then not different from the hydroceles of later life.

3. *Encysted Hydrocele or Hydrocele of the Cord.*—These are most frequently observed in the inguinal region of young infants.

They are entirely independent of the tunica vaginalis testis and are situated a great deal higher up, either near the external ring or in the inguinal canal. They usually appear as small cysts that are moveable, and can be pushed up and down in the canal or made to appear through the ring.

They are sometimes mistaken for supernumerary testes, and perhaps more often for hernias, but that mistake ought not be made as they are too freely moveable to resemble the latter.

Interesting and curious combinations of the cystic dilatation of these canals sometimes occur. Thus, the inguinal process of the peritoneum, as well as the vaginal process may undergo dilatation though the funicular process remains almost closed, giving rise to a kind of double hydrocele—bilocular or wallet-shaped or gourd-shaped hydrocele. In such cases the scrotal pouch is pyriform, as in ordinary hydroceles, but the upper pocket presents a variety of different appearances according to circumstances, sometimes forming a rounded or oval ampoule. It may appear only in the groin, or may dissect its way behind the parietal peritoneum toward the umbilicus or downward into the pelvis.

Congenital Inguinal Hernia in the Male

Congenital inguinal hernia is the passage of abdominal viscera into or through the inguinal canal. It is an accident that results from persistence of some part of the peritoneo-vaginal process of the peritoneum.

How frequently all or parts of this canal remain open is shown in the following tabulation of the observations of different authors:

I. NORMAL CHILDREN

Reporter	Cases observed	Canal open				Canal closed			
		Males		Females		Males		Females	
		R.S.	L.S.	R.S.	L.S.	R.S	L.S.	R.S.	L.S.
Camper............	70 new-born	14	8	o	o				
Zuckerkandl........	100, first 3 months *Bilateral*								
	20	12	5	o	o				
Fere..............	62, less than one month								
H. Sachs..........	....	..	..	..	..	..	34		

Canal open in 59% during the first four months.
Canal open in 44% during the fifth month.

II. Children with Hernia

Reporter	Cases observed	Canal open				Canal closed			
		Males		Females		Males		Females	
		R.S.	L.S.	R.S.	L.S.	R.S.	L.S.	R.S.	L.S.
Berger............	424 *Bilateral*								
	52	253	119	0	0				
Kirmisson.........	120								
	12	60	45	4	8				

Notwithstanding the frequency with which the canal is thus shown to be open, it is a very rare thing for children to be born with hernia. Wrisberg saw two cases, and Chaussier one. Of course it may be said that there is predisposition to it in all, but the actual occurrence of the hernia, in cases in which it does occur, is postponed for several months. It seems, therefore, clear that other factors than the common persistence of the canal must play a part in the etiology of the condition.

It is customary to divide the hernias of children and adults according to the anatomical condition and relation of the parts, as follows:

1. Congenital hernia.
2. Infantile hernia
   (a) Infantile hernia proper
   (b) Encysted hernia.
3. Funicular hernia.

These classes have nothing to do with the time at which the hernias make their appearance as their names suggest but solely with the anatomical relations of the parts concerned.

I. *Congenital Hernia.*

In this variety, the intestine, usually the lower part of the small intestine, rarely a part of a Meckel's diverticulum, simply follows the testis through the peritoneal prolongation into the scrotum, where it lies in immediate relation with it. In the inguinal canal the spermatic cord is usually below and behind the intestine; in the scrotum, the testis lies in front and a little to the inner side of the intestine.

The sac of such a hernia, when carefully examined usually shows several presumably natural, more or less marked constrictions, which correspond to the points at which natural obliteration should have taken place. The first is at the internal abdominal ring, the second at the external ring, and the third in the scrotum. It is well to be acquainted with them in view of subsequent possible strangulation.

II. *Infantile Hernia.*

(a) *The Infantile Form of Infantile Hernia.*

This is characterized by closure of the intestinal conduit at the internal abdominal ring only, the remainder remaining open. In such a case if hernia should subsequently develop, through pressure upon the yielding septum, the effect would be to carry the adjacent peritoneum down into the scrotum behind the tunica vaginalis. An examination of such a case would show the scrotum to contain three layers of peritoneum in front of the testis, two belonging to its tunica vaginalis, and one composing the sac of the hernia.

(b) *The Encysted Form of Infantile Hernia.*

Here again the closure of the canal has taken place only at the internal abdominal ring, but the lower part is not only open, but must be distended with a certain

amount of fluid. Any descending loop of intestine under these circumstances does not push before it a new layer of peritoneum as in the preceding case, but invaginates the vaginal process into itself. Such a hernia is found upon dissection to be surrounded on all sides by two layers of peritoneum, the outer being the lower portion of the vaginal portion in what may be considered its normal position, the other, constituting the sac of the hernia, the upper portion of the same invaginated into itself. Kirmisson points out the danger that at any moment the invagination may perforate, the intestine find itself in the cavity of the tunica vaginalis, and strangulate at the newly formed orifice.

III. *Funicular Hernia.*

In this variety, the testicular conduit has closed only at its lower portion, near the epididymis, thus perfecting the tunica vaginalis, but leaving the funicular portion open. The descending intestine, in such cases cannot come into relation with the testis because of the partition that divides off the tunica vaginalis.

Clinically this form closely resembles simple congenital hernia but can usually be differentiated from it because the intestine can rarely descend to the bottom of the scrotum, and the testis can be felt below.

In addition to these generally recognized varieties of hernia, others to which reference must be made, have been from time to time described.

Inguino-properitoneal Hernia.—This was first described by Parise, in 1851, and later studied by Streubel. Kronlein found only 15 out of 23 cases to be of manifestly congenital origin.

It is characterized by the passage of the intestine through the inguinal canal and into the scrotum, and at the same time the formation of a second pouch extending from about the position of the external abdominal ring, anteriorly between the peritoneum behind and the external abdominal ring in front. It is on account of the position of this pouch that it receives its name.

Inguino-interstitial Hernia.—This occurs as a complication of ectopia testis, and was first described by Danse in 1835, though it did not receive much attention until more carefully studied by Tillaux. It has two distinctive peculiarities; first the testis, being ectopic, remains in the inguinal canal; second, the intestine also remains in the inguinal canal. Under these circumstances the canal may undergo enormous dilatation, largely in an upward direction, towards the anterior superior spinous process of the ilium and the umbilicus. In one case observed by Tillaux, the sac contained no less than 30 centimetres of intestine.

In this case, the sac of the hernia developed in the thickness of the abdominal wall in front of the aponeurosis of the external oblique and behind the transversalis and its fascia. In such hernias the testis is sometimes situated immediately below the external orifice of the canal which it obliterates, sometimes on the inferior surface of the sac of the hernia.

No matter what course the testis takes in its descent, it is possible for it to be followed by the intestine, and complicated by hernia. As the normal descent is through the inguinal canal, the inguinal hernia is naturally the most frequent complication, but in those cases in which the course of the testis is abnormal and peculiar, it may be followed by the intestine, so that cruro-scrotal and perineal hernias occur.

In some cases the descending testis becomes arrested in the inguinal region—ectopia—but the intestine keeps on and descends into the scrotum. In some cases the fixation of the testis in the ectopic position interferes with the subsequent occurrence of hernia, sometimes the hernia develops just the same, and sometimes the ectopic testis prevents later reduction of the hernia. Among the most instructive cases are those in which the testes remain high up in the abdominal cavity, though the intestine descends into the scrotum on both sides. Bramann adduces such cases as evidence of the complete independence between the testicular and intestinal migration.

Congenital Inguinal Hernia in the Female

The mesorchium, or peritoneal fold that covers the testis in the male, has its homologue in the mesovarium in the female. In both sexes it is composed of fibrillar connective tissue, containing many smooth muscle cells, and is therefore contractile. It becomes the gubernaculum testis in the male, the round ligament in the female. This round ligament of the uterus, behaves in very much the same manner as the gubernaculum of the male, that is, it perforates the abdominal wall, and descends, not into the scrotum, but into the labium magus which is its homologue, and as it does so, carries with it a narrow canal of peritoneum, the canal of Nuck, which affords opportunity for the occurrence of inguinal hernia, as well as for the other malformations of the region already pointed out as occurring in the male. But as the ovary does not normally pass through the inguinal canal, the canal of Nuck is more prone to early closure than the vaginal process of the male. It is probably on this account that congenital hydroceles and congenital inguinal hernias are less frequent in the female sex. In 1841 Malgaigne declared inguinal hernias to be the more frequent form in the female, but he seems not to have convinced the profession, and many authors still believe the contrary.

One or both ovaries may prolapse into the canal of Nuck, and occasion ovarian hernias, followed by symptoms not unlike those occurring in ectopia testis—neuralgic pain, etc. In the abnormal environment, they may also undergo atrophic changes or develop neoplasms. Such descent of the ovaries may be followed by simultaneous or subsequent descent of the intestine, and associated hernia.

Double Vagina; Double Uterus; Uterus Bicornis, etc.

These are among the most simple congenital malformations to understand when their embryological explanation is at hand, and among the most incomprehensible without it.

At the time that the mesonephros is developing, and its tubules forming their connection with its duct, the Wolffian duct, new tubular structures are appearing on each side of the embryonal body, in close juxtaposition to it. These are the ducts or tubes of Müller. It is not definitely known from exactly what structures they arise. Sedgwick supposed that the anterior part was derived from the pronephros, and that the posterior part split off from the Wolffian duct, a theory of origin entirely in keeping with what takes place in certain of the lower animals. According to McMurrich, the appearance of the ducts is foreshadowed by a ridge or fold on the ventral surface of the Wolffian body, from the under surface of the diaphragm to the uro-genital sinus. He gives the exact mode of formation as follows: "Near the anterior end of the mesonephros there grows into the fold (above mentioned) an evagination of the peritoneal covering of the Wolffian ridge, and by the proliferation of its tip, this evagination gradually extends downward in the substance of the ridge, and in embryos of 22 mm. has reached the uro-genital sinus. As they approach the sinus, the right and left evaginations, or Müllerian ducts, gradually approach one another and finally fuse together and form a single tube at the lowest part of their course. But they remain distinct above, each tubule retaining its opening into the peritoneal cavity."

The origin of the structures, however, is of little importance in comparison with their destiny, and that is known very well. In the male sex they are to disappear, except for the upper and lower extremities, the former of which becomes the hydatid of the epididymis, the latter the sinus pocularis or uterus masculinus. But in the female they are to assume vastly greater

importance, the entire structures surviving, their upper ends to become the hydatids of Morgagni, the middle portions the Fallopian tubes, and the lower portions, fused together, to form the uterus and vagina.

It is about the eighth week of embryonal life that the opposed surfaces of the two Müllerian ducts become united, and the intervening septum disappears, so as to form a single tube, which, for a time ends blindly and is continued to the uro-genital sinus as a solid cylinder of cells, the cord of Thiersch. This lumenless segment of the fused Müllerian ducts is the part from which the vagina will subsequently be developed. The final lumen of the genital canal is formed through the activity of its cells.
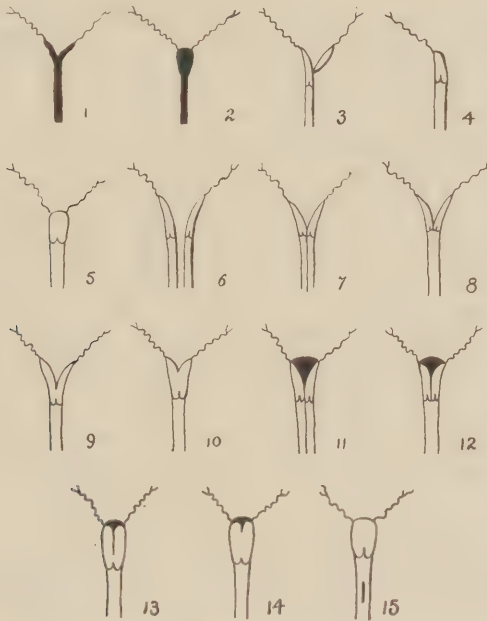

FIG. 42.—Diagram of the congenital malformations of the uterus and vagina. 1 and 2, Symmetrical hypoplasia; 3–5, asymmetrical aplasia and hypoplasia; 6–10, incomplete unions with visible separations; 11–15, externally complete and internally incomplete union of the embryonal parts. (*Aschoff.*)

Should arrest of development in this region occur early and before the fusion of the tubes there may result two uteri and two vaginae side by side. If it occur later, the malformation may be partial, according to the following scheme arranged by Aschoff:

Malformation of the Female Genital Tract.
    I. Rudimentary development.
        A. Symmetrical Aplasia and Hypoplasia.
            1. Aplasia corpus uteri.
                Complete absence of the body of the uterus is extremely rare. The Fallopian tubes and the vagina may exist.
            2. Uterus bicornis solidus.
                The Müller's tubes have come together but are solid, and usually insufficiently developed. (Diagram, 1.)

3. Uterus rudimentarius excavatus.
  The cavity exists only in the upper and middle parts.   The vagina is absent or consists of a solid cord.   (Diagram, 2.)
B. Asymmetrical Aplasia and Hypoplasia.
  1. Uterus bicornis cum cornu rudimentario.
    One Müller's tube is fully developed, the other is attached to it as an accessory structure forming the other uterine horn, from which it may be entirely shut off. Through migration of semen and the impregnated ovum into the rudimentary horn, pregnancy may occur there.   (Diagram, 3.)
  2. Uterus unicornis.
    Only one of the tubes of Müller is developed.   Rudiments of the tube and ovary may be present on the other side.   (Diagram, 4.)
  3. Vagina unilateralis.
    The vaginal portion of one Müller's tube is missing, the other is well-formed. (Diagram, 5.)
  4. Tuba unilateralis.
    Unilateral absence of the tube.
II. **Incomplete union of Müller's ducts.**
  A. With visible separation.
    1. Uterus duplex separatus.
      Complete separation of both passages.   (Diagram, 6.)
    2. Uterus didelphys cum vagina septa.
      The uterus is divided; the vagina united, but with a partition corresponding to the line of fusion.   (Diagram, 7.)
    3. Uterus bicornis duplex.
      The vagina is complete, but the fusion is incomplete at the cervix, and the isthmus and body are divided.   (Diagram, 8.)
    4. Uterus bicornis unicollis.
      Complete union of the vagina and cervix; incomplete union of the isthmus and separation of the halves of the body of the uterus.   (Diagram, 9.)
    5. Uterus arcuatus.
      Complete union of the vagina, cervix and isthmus; incomplete union of the corpus. Moderate cases are frequently described as uterus planifundus.   (Diagram, 10.)
  B. With externally perfect but internally incomplete union of Müller's tubes.
    1. Uterus bilocularis septus cum vagina septa.
      A complete septum divides both vagina and uterus.   The vagina may be closed. (Diagram, 11.)
    2. Uterus septus duplex.
      The uterus is divided by a septum but the vagina is perfectly formed.   (Diagram, 12.)
    3. Uterus septus unicollis.
      The vagina and cervix are perfectly formed, but the isthmus and corpus of the uterus are divided by a septum.   (Diagram, 13.)
    4. Uterus subseptus.
      The vagina, cervix and isthmus are perfectly formed, but there is a longer or shorter septum in the corpus.   (Diagram, 14.)
    5. Vagina septa.
      The vagina is imperfectly formed, a septum somewhere dividing it.   The uterus is perfect.   (Diagram, 15.)

Atresia Vaginæ: Atresia Colli Uteri

The account of the formation of the uterus and vagina given in the last section probably did not tell the whole story, but only so much of it as was necessary to explain the more frequent malformation of those organs.

Perhaps the reader will recall that in the explanation of hypospadias in the female, mention was made of the participation of the uro-genital sinus in the formation of the female urethra. Retterer is the chief exponent of the theory that part of the vagina, and perhaps part of the uterus may be derived from the sinus, and describes the development of the parts thus:

"The posterior part of the uro-genital sinus, that part into which the ducts of Müller insert, grows downward toward the level of the perineum, and at the same time a kind of spur descends between the ducts inclosed in the cord of Thiersch and the lower part of the bladder; a membranous fold projects from each side of the sinus, to meet near the middle line and separate a short length of the sinus as the female urethra, leaving the posterior part, also short, but of greater diameter, to be the future outlet of the female genital apparatus by joining with the now lengthening ducts of Müller which form the remainder. At the time that this takes place the conjoined ducts of Müller have become flattened and their epithelial linings have undergone proliferation by which their cavities are entirely closed so that they are no longer tubes but cords. Near their connection with the short tubular structure originating from the uro-genital sinus, which is almost at the surface of the genital orifice, a semicircular fold of tissue grows from below upward, partly closing the canal; it is the hymen."

Atresia may result from arrest of development by which the canallization of the vagina or cervix uteri is prevented, or, as is more frequently the case, from complete closure of the mouth of the canal by excessive development of the

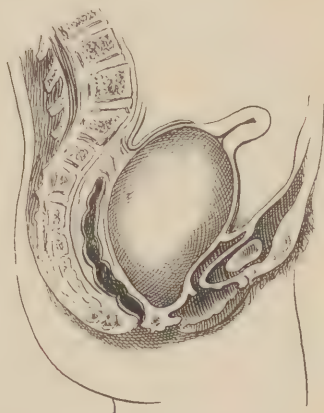FIG. 43.—Uterine cervical atresia with hematometra. (*Redrawn from Kirmisson.*)

FIG. 44.—Vaginal atresia from imperforate hymen with hematocolpos. (*Redrawn from Kirmisson.*)

hymen. The latter is scarcely an arrest of development, however, and is only introduced at this point because it brings the more frequent form of obstruction into line with the actual arrests of development and facilitates discussion of the resulting condition. For the same reason it may be well to point out that occasional cases occur in which the orifice becomes closed through vulvar and vaginal inflammatory conditions later in life. It is not always possible, however, to determine the exact etiology of such obstructions. Thus H. A. Kelly has reported a case in which well formed labia were united by a dark colored membrane upon which was a well marked central raphae, the genital orifice being represented by an opening only 3 mm. in diameter.

Cases of atresia usually escape observation until puberty arrives and the menses are expected. The other indications of menstruation are present, but no blood appears, because there is no outlet for its escape. Repeated monthly periods occur, and become more and more painful, still without the appearance of any blood. In such cases the menstrual blood, is accumulating behind the obstruction, and dilating the passage, either the cavity of the uterus, which occasions uterine colic, or in that of the vagina.

In such cases an examination reveals the presence of a considerable median hypogastric tumor, ascending toward the umbilicus which it may in fact reach. It is the collection of menstrual blood. If the external genitalia be examined, the dark colored hymen may be seen bulging between the labia. All that is then necessary is to perforate the membrane, when the blood will escape. But if the obstruction be higher up, and depend upon imperforation of the vagina or cervix, no external evidence will be found, the diagnosis is more difficult, and more radical operative methods will be necessary for its remediation.

VIII. In the Mammary Region

Supernumerary Mammary Glands

First making their appearance in embryos of 9 mm. and becoming distinct in those of 15 mm., are two lines of the ectoderm that pass from the axilla to the groin along the edges of the primitive abdominal wall.

They were first pointed out by Schultze, by whom they were designated "milch leisten" or milk lines. Schmidt, later showed that they were not peculiar to the lower animals, but occurred also in man. Along these, at regular intervals the epithelium heaps up into little eminences that are the rudiments of the future mammary glands, and Schmidt found that in human embryos they were numerous upon the thorax and abdomen. Under normal conditions, in human embryos, all but two, one on each side of the thorax are eventually lost. If this extinction of the rudiments does not occur, that is, if development is arrested, a greater than normal number of mammae will result, and supernumerary glands occur.

IX. In the Alimentary Canal

The alimentary canal begins its existence very early in embryonal life as an elongate, broad tubular structure, extending from the head end to the tail end of the embryo, and constricted from the yolk sac by the growth of the somatopleure. This primitive gut tube, being outgrown for a time by the surrounding structures, appears to diminish in calibre without increasing in length, and becomes a long slender tube, closed anteriorly by the pharyngeal membrane, and posteriorly by the anal membrane.

The chief thing to remember in the present connection is that there is no break in the continuity of the tube. The changes that subsequently take place are the result of a somewhat sudden increase in length, by which it outgrows the surrounding organs, and by dilatation of certain of its parts, which become

differentiated into the oesophagus, stomach, small and large intestine. If, therefore, a break in its continuity, or a stenosis of its lumen occurs, there is no clear embryological explanation other than the possibility that the particular part thus affected may have failed to attain to its normal size, as the result of extension, torsion, or malnutrition.

Stenosis of the Oesophagus

This form of congenital malformation usually occurs at the junction of the middle and lower thirds, where a constriction separates the structure into two portions connected by a fibro-muscular band. The upper part usually forms a pouch, the lower a slender tube, pointed above, and sometimes connecting with the trachea through a fistula. Such cases cannot live, as there is no way for food to enter the stomach. It is supposed that they are the result of excessive development of the membranous separation between the primitive gut and the respiratory bud, at the time the formation of the respiratory system is begun.

Hour-glass Stomach

This pecularity appears as a constriction of the circular muscle fibres somewhere between the cardia and pylorus, and may be so slight as scarcely to excite comment, or so marked as to divide the organ into two separate pouches of equal or unequal size, connected by a narrow passage.

As cases are frequently first recognized at autopsy late in life, it is probably of slight significance. Congenital cases are not always to be differentiated from those acquired after birth through cicatrization following ulceration of the stomach.

Pyloric and Duodenal Stenosis

Pyloric and duodenal stenosis are among the most important congenital malformations of the alimentary tract, and have the advantage that they are operable, so that successful surgical intervention makes life possible where otherwise there was no hope.

The stenosis is usually either at the pylorus itself, or in the duodenum at about the position of the papilla of Vater. It may take the form of simple narrowing, or complete obstruction. The upper and lower segments may be connected by a fibrous cord without a lumen, or by a cord with a minute canal through which a fine probe can be passed. There is usually considerable dilatation above, and contraction below the seat of obstruction in cases without complete closure.

Various explanations have been given, in an endeavor to account for the malformation. Some cases have been found to be associated with hypertrophy of the muscle of the pyloric ring, others with what were regarded as adenomatous enlargement of the mucous membrane of the neighborhood of the obstruction. Some have been referred to spastic contraction of the muscle of the pyloric ring. Many cases, and especially those situated in the duodenum are without satis-

factory explanation, and it is for them that the theory of arrest of development of the digestive tube seems applicable.

Stenosis of the Ileum

Stenosis of the ileum may occur at the junction of the ileum and jejunum, at the point of origin of the omphalo-mesenteric duct, and at the junction of the ileum and caecum. In addition to these seats, a few cases have occurred with multiple stenoses in no particular regions.

Intestinal stenoses may be partial or complete, that is, the tube may be simply narrowed, or completely closed, the upper and lower segments being connected by a more or less fibrous cord without muscular tissue. Above the uppermost obstruction there is usually considerable dilatation, supposed to be the result of ingestion of the amniotic fluid, rather than of the small amount of food that the infant took before death.

Stenosis of the Colon

These are rare, and as the greater number of them seem to occur low down, easily become confused with the atresia recti.

B. DEPENDING UPON STIMULATION OR PERVERSION OF THE DEVELOPMENTAL FORCE: EXCESSIVE DEVELOPMENT

If in the course of embryonal development, some part or member outgrows its fellows so as to exceed all standards of size and assume a gigantic grotesqueness, it becomes difficult to escape the conviction that it is the result of abnormal stimulation of the developmental force.

If instead of developing the usual number of parts or members, some are excessive, the excess may be explained upon the assumption that the developmental force has been perverted.

Thus, if a child be born with two thumbs, or with six or seven fingers and it is found that the malformation is not only congenital but also hereditary, and runs through several generations of the same family, it can scarcely be attributed to accident, but must be referred to conditions intrinsic in the germ-plasm.

Developmental excesses when analyzed yield the following possibilities:

1. Stimulation of development, manifesting itself in increased size of certain parts.

2. Stimulation of development manifesting itself in increased number of parts.

3. Inhibition of development through which local excesses may appear.

It is well known that during embryonal development certain things take place at definite times, and in regular order, now progressing rapidly, now slowly, but what determines the alternations and sequences, no one has yet found out. Appearances are very deceptive and from them alone erroneous deductions would be inevitable. For example, polymastia, or excessive number of mammary glands seems to result from the failure of the excessive rudiments to be suppressed. It is therefore the result of arrested development, but to one

unfamiliar with the natural process of mammary development, it certainly appears as an excess of development. That opinion is justified in so far as the supernumerary glands do represent an excess of glandular tissue, but had the excessive primitive rudiments been suppressed at the right time, future development would have progressed according to the regular type, and only the normal

FIG. 45.—Well-marked right rudimentary left seventh cervical rib. (*Henderson.*)

number of glands appeared. If the reader suppose polymastia to be an atavistic phenomenon, the case is in no wise changed, for what is the higher development to be referred to except the suppression of the superfluous rudiments.

SUPERNUMERARY—(CERVICAL)—RIBS

Human beings are normally provided with 12 pairs of ribs, all of which arise from the dorsal vertebrae. When a rib is carefully studied, it is found to be no

more than an exaggeration of certain of the vertebral processes, and if the vertebrae be examined, it will be found that the modification of their processes into ribs is not difficult. The lower cervical vertebra, for example, are found to have transverse processes consisting of a base implanted on one side of the body, and a summit consisting of two tubercles, one anterior the other posterior. The osseous point that forms the anterior tubercle, is the homologue of a rib. Under normal conditions of development, the two tubercles unite to complete the transverse process of the vertebra; under abnormal conditions exaggerated development of the anterior tubercle may take place and a supernumerary rib appear.

Supernumerary ribs in human beings are almost always cervical, and are the result of the costal tubercle of the seventh cervical vertebra remaining free. In extremely rare cases it is said that similar formations may arise from the sixth and even from the fifth cervical vertebrae.

The nature of the excess is debatable; some look upon it as a manifestation of atavism, and hence would bring the malformation in line with arrest of development—i.e., loss of developmental inhibition. It is true that many lower animals have a greater number of ribs than man, but there are many objections to carrying the theory of atavism too far.

Cervical ribs are always congenital, and occur, according to A. S. Taylor in the proportion of 1:300 normal individuals. The supernumerary structure may escape detection altogether, and is rarely detected until adult life. Of 139 cases collected by Gruber and Pilling, 67% were bilateral, and all arose from the seventh cervical vertebrae, except one case reported by Karg and Hauswirth which arose from the sixth. Morphological studies by Blanchard resulted in the following divisions:

1. The cervical rib is complete, passing from the transverse process of the seventh cervical vertebra to the sternum with which it articulates between the clavicle and the first true rib.
2. The cervical rib is complete, but its cartilage does not fuse with the sternum, but with that of the first rib.
3. The cervical rib exists only in the form of two extremities connected by a fibrous cord.
4. The extremities of the rib alone exist, there being no fibrous cord connecting them.
5. The anterior extremity of the supernumerary rib may fuse with the first rib which appears to bifurcate in the form of the letter Y at its posterior extremity.

When the length of the seventh cervical rib exceeds 5 or 6 centimetres it is crossed, above, by the subclavian artery; when it is shorter, the artery fails to come into relation with it and passes over the first rib as usual. The brachial plexus of nerves may be elevated and compressed.

In consequence of the disturbed anatomical relationships, the presence of a cervical rib may be clinically indicated by certain fairly distinct nervous and vascular phenomena. The best marked of these consist in weakness and numbness of the entire upper extremity, with formication and cramps. The arm may be notably weaker than its fellow of the opposite side, and may be so cool that the patient desires to have it covered. In more severe cases there may be passive congestion and edema of the arm.

In the worst cases there may be aneurysmal dilatation of the artery, and more or less thrombosis. Hodgeson and Cooper have reported cases in which superficial gangrene of the fingers occurred, and closely resembled Raynaud's disease, from which they could only be differentiated by examination with the X-rays. Some question whether all cases of Raynaud's disease may not be the result of undetected cervical ribs.

Arrou, Fredet and Demarest point out that the lancinating pains that sometimes characterize the presence of cervical rib, although they usually follow the course of the compressed nerves, and radiate down the arm, may extend into other regions—to the shoulder and ear, along the course of the musculocutaneous and circumflex nerves of the arm of the affected side.

Sometimes, in order to avoid pain, the arm has to be kept in some definite position, and some patients, in order to sleep are compelled to keep it adducted. P. Marie, Crouzo and Chatelin have observed muscular atrophy of the arm of the affected side. One case observed by Tillman suffered from hoarseness and dysphagia. Unilateral cervical rib may be associated with scoliosis of the lower cervical and upper dorsal region the convexity of the curve being directed toward the opposite side.

The diagnosis may be difficult without the employment of the X-rays. Some cases with suggestive symptoms enable the diagnosis to be made by palpation alone, a hard swelling that can be followed to the vertebral column being present in the supra-clavicular region. In all cases, however, it is best to depend upon the X-rays.

Operation is immediately indicated in cases with severe symptoms, but may be postponed when they are mild. However, as the symptoms are said sometimes to develop unexpectedly, it may be good practice to remove the superfluous structures in all cases.

Supernumerary Vertebrae

These are of very rare occurrence, but the knowledge of their possible presence is of some importance in attempts to correct spinal curvatures.

Fortunately they most frequently occur in the sacral and coccygeal regions where they are either of no importance, or can be removed (coccyx) if necessary. Indeed, most supernumerary vertebrae pass undiscovered during the life of the individual, and first come to observation in the dissecting room, or when the skeleton is being prepared in the anatomical laboratory.

Those requiring particular attention are of wedge shape, and are situated in the upper lumbar or lower dorsal regions. They occasion irremediable scoliosis, the explanation for which can only be found through X-ray examination. On this account it would be good practice to make such examinations of the spinal columns of all cases of that deformity.

Tails and Tail-like Appendages

In the second month of embryonal life the tail of the embryo contains rudiments of seven vertebrae, of which all but three disappear by absorption, leaving the associated tissue of the chorda dorsalis persisting for a considerably longer

time.   Whether as the result of atavism, or for some other reason not yet recognized, the absorption of the superfluous elements sometimes miscarries, and the tail persists and develops.

The form of the resulting appendage depends upon the time at which the suppression of its tissue was interrupted.   Thus, if at a time anterior to the

Fig. 46.—Infant with a "soft tail," *i.e.*, one without bones, attached in the mid-line about 1 cm. below the tip of the coccyx.   It was covered with normal skin containing fine hairs and was well vascularized.   Three distinct portions or segments could be made out.   Two weeks after birth the tail was 4.4 cm. long, and at the age of two months it had grown to the length of 5 cm.   The most remarkable characteristic was its movability.   When at rest it would lie extended in the midline, but the mother saw it bend through an angle of 180°, its tip pointing towards the head.   When the child was irritated and cried or coughed the tail would contract markedly.   The distal portion could be drawn in sharply, telescoping the middle segment which became shorter and thicker.   The tail was removed when the child was about 6 months old.   (*Harrison*.)

disappearance of the rudimentary vertebrae, the appendage will be much like the tail of one of the lower animals, and will contain caudal vertebrae; if a little later, will be tail-like, but contain bony nodules; if still later, it may be a mere fleshy appendage.   The latter is the most frequent condition, and the mass of tissue may be so amorphus as to become confused with the tumors of the region. Dissection of the appendages brings out a structure in correspondence with

their configuration. The well-formed tails not only have their complement of bones, but also the ligaments, tendons, vessels, muscles, nerves, etc. that go to make up a definite member. The amorphus masses may also show structures without arrangement or order.

All tail-like appendages should be removed at an early period of life, as they are serious embarrassments later in life.

Supernumerary Digits—Polydactylia

Soon after their appearance, the limb buds develop terminal expansions of flattened shape, something like paddles, or as Kirmisson describes them, like "battledores," which are to become the hands and feet respectively. Across the middle of each of the paddles a transverse groove soon appears to mark the line of separation between the palm or sole respectively, and the digits, which later become marked out through the appearance of four longitudinal grooves. If fewer than four such grooves occur, there will be fewer than five digits; if more than four grooves, more than five digits. The primary error, then seems to be in the initial markings. There is no way of determining why differences in the markings should occur, but the fact that the condition is distinctly hereditary, indicates that it results from some circumstance affecting the germplasm.

In addition to the commoner form of polydactylia, in which the additional digits are in line with the regular series, there is another in which the supernumerary members are irregularly attached to their fellows. It is just as hereditary as the other.

One or two supernumerary fingers in regular and orderly sequence with their fellows do not seriously interfere with function or destroy symmetry but when, as sometimes happens, there are ten or twelve, the hand is rendered useless through their excessive number and small size.

Malformed supernumerary fingers are most apt to occur out of the regular line, either on the radial side, where they are thumbs, or the ulnar side where they are little fingers. The resemblance is sometimes complete, sometimes slight, and they may be so malformed as to appear only as small fleshy tissue masses, with or without a suggestion of a nail. In some cases the condition is bifidity rather than duplication: thus, two thumbs, each with its separate phalanges, and its own well-formed nail may arise from one metacarpal bone, or the terminal phalanx is divided into two similar endings, each with its own nail. In such cases of dichotomy, the two members move together, having their tendons in common.

A much more rare malformation, not, indeed falling correctly in the present class is the occurrence of an extra phalanx in the thumb, thereby increasing its length and giving it a new joint. Kirmisson has seen two cases of this kind, in each of which inherited predisposition was found. Sappey explains the occurrence as the result of interference with development. There are originally as many segments to the thumbs as to the other digits, but as development proceeds, the metacarpal and adjacent phalanx fuse and reduce the joints from three to two. If this fusion is arrested, the member retains its original number of joints.

Supernumerary digits should always be removed if the operation will improve the symmetry and usefulness ont he hand.   Cases of exaggerated deformity should be given careful consideration, and no sacrifice made that may be injurious.   Thus, there are cases of eight digits on the same hand, so arranged as to make each half oppose the other.   Such a member is useful as it is, but becomes almost useless if four of the superfluous digits are removed simply for cosmetic reasons.

FIG. 47.—Congenital hypertrophy of the left middle finger.   (*Jeffries and Maxwell.*)

Partial amputations should be avoided and amputation incisions should be made to pass through the joints as sometimes regenerative growth takes place from the remaining cartilage.

CONGENITAL LOCAL HYPERTROPHY

In conditions of this class the excessive development takes the form of local excesses frequently spoken of as partial giantism.   It is always congenital, so that the time at which it begins, if it did not occur simultaneously with the development of the part itself, cannot be determined.   The distribution of the tissue excess is different in different cases, and gives rise to most striking deformity.   Not infrequently it takes the form of gigantic size of one or several of the extremities—fingers or toes—to which it may be limited, or from which it may gradually fade away into the normal tissues of the adjacent parts.   Sometimes, on the contrary, it manifests itself through the development of an unaccountable asymmetry of the more centrally situated structures, making the face lop-sided, or giving the trunk a lateral massiveness.   Where not definitely limited it sometimes becomes confused with elephantiasis, from which there

should be no difficulty in differentiating it because of the acquired character of that disease.

It is probably most striking and therefore perhaps most typical when it affects the digits, where it sometimes causes the attainment of several times the normal dimensions, with almost perfect preservation of the symmetry.

Curling in 1845 collected seven cases, one his own. In the latter the middle finger of the right hand, and the fore and middle fingers of the left hand were affected, and of great size.

Fig. 48.—Congenital hypertrophy of the toes. The two small members on the left are the great and first toes, the three on the right the middle, fourth, and little toes. (*Case of Dr. J. P. Mann.*)

In a case seen by the author and J. P. Mann, the patient was a boy aged 12 years, who, at birth was observed to have the deformity, that brought him later under observation and caused him to submit to an operation. His left foot was remarkable through the enormous size of its outer three toes, each of which was about twice its normal length, and three times its normal thickness. The proportions were otherwise not notably disturbed, and each digit was provided with a well-formed nail proportional to its size. An X-ray photograph showed the internal structure to correspond with the external appearances, the bones also being well proportioned to the size of the massive digits. The disturbance affected the phalanges, the metatarsals and the outer tarsal bones, and was accompanied by an increased thickening of the soft parts that extended

up the outer side of the leg to the knee. The impossibility of wearing paired shoes, and the disfigurement caused by the wearing of one large and one small shoe, drove the patient to seek relief. The giant toes were amputated, and the foot trimmed to a size compatible with the wearing of a shoe mated with that of the other foot.

As such exaggerated members are always useless because of their dispro-portions, they can be sacrificed without hesitation, and usually with benefit.

In cases in which the hypertrophy involves more centrally situated structures, as one side of the face, nothing can be done to restore the symmetry.

No satisfactory explanation of the condition has been offered.

II. DEPENDING UPON ACCIDENTAL DISLOCATION OF TISSUE DURING EMBRYONAL DEVELOPMENT (CHORISTA)

The distinction between the conditions to be considered under the present major heading and the next one is not entirely satisfactory or accurate, and the adopted classification is to be looked upon as practical rather than as scientific.

Any tumor-like formation conceived to arise through the delayed develop-ment of an aberrant primordium, falls in the group to which Albrecht applied the name *choristoma*. If it can be shown that the separated primordium even-tuates in autonomous tumor formations, the term *choristoblastoma* is appropriate.

The following outline gives a general idea of the various forms assumed by developmental defects of this nature.

A. The dislocated embryonal rudiment may eventuate in undifferentiated miscellaneous tissue masses in otherwise well-formed structures.
  1. The dislocated rudiment is ectodermal.
      Cholesteatoma
  2. The rudiment is mesodermal.
      Mixed tumors: Mammary, ovarian, palatal, pharyngeal, pituitary, renal, salivary, testicular, thyroid, tonsillar, uterine, vaginal, vesical, etc.
B. The dislocated fragment may eventuate in a definite structure.
  1. A portion of the primitive rudiment may become surrounded by the perfected organ in which it appears as a circumscribed node or nodule.
      (a) The rudiment is ectodermal
          It is located in the skin
              Dermoid cyst
          It is located in the mammary gland
              Fibro-adenoma
      (b) The rudiment is endodermal
          It is located in thyroid body
              Fetal adenoma
      (c) The rudiment is mesothelial
          It is located in the adrenal body
              Adrenal adenoma—Hypernephroma (?)
  2. A portion of the primitive rudiment of one organ may become inclosed in the sub-stance of another organ as a node or nodule, or be separated from it widely.
      (a) The rudiment is endodemal
          It is derived from the pancreatic primordium.

It is embedded in the tissues of the stomach, duodenum, jejunum, ileum, Meckel's diverticulum, mesenteric fat, great omentum, capsule of the spleen, hilum of the spleen.

It is derived from the thyroid primordium

It appears embedded in the tongue—lingual thyroid—larynx, trachea, internal auditory meatus or connected with the hyoid bone or aorta.

(b) The rudiment is mesenchymal—adrenal

It is derived from the adrenal primordium

It is embedded in the tissues of the kidney, liver, ovary, testis, pancreas, spleen, solar plexus or it may be upon the surface of the epididymis, paradidymis, spermatic cord, Fallopian tube, various blood vessels, etc.

It is derived from the liver

It appears in the ligaments of the liver

It is derived from the ovarian primordium

It usually lies near the organ proper in the broad ligament

It is derived from the endometrium

It is embedded in the tissues of the uterus, recto-vaginal septum, Fallopian tube, round ligament, hilum of the ovary, utero-ovarian ligament, utero-sacral ligament, sigmoid flexure, rectus muscle or umbilicus.

3. The primordial rudiment becomes so divided as to give rise to multiple—supernumerary organs.

Such may be derived from the spleen, pancreas, ovary.

CHOLESTEATOMA: "PEARLGESCHWULST:" MARGARITOMA"

Most text-book descriptions of cholesteatoma are vague and unsatisfactory, when not more or less contradictory, and leave the reader uncertain upon almost
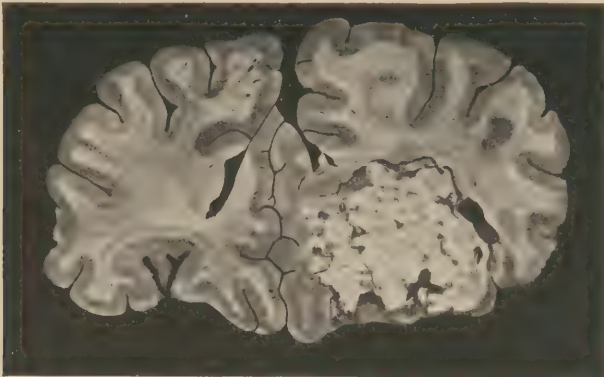
FIG. 49.—Cholesteatoma. A mass of cornified epithelial-cells which has been slowly formed and pressed into the brain. (*Mallory, "Principles of Pathologic Histology."*)

every particular. This seems to depend upon resemblances that have led to certain lesions being grouped together without sufficiently careful consideration of their diverse origins.

To appreciate this it is necessary to refer to the original descriptions in the writings of Cruveilhier and Müller, and the later analysis of their work by Virchow.

Cruveilhier, examined a tumor that occurred in the brain of a girl 18 years of age, filling the entire median basilar fossa. It was covered by the arachnoid, had a metallic lustre like dull silver, or a pearl of the first water, and a nodular surface as though composed of an agglomeration of little pearls of different sizes. The pearly lustre was, however, only superficial, and the cut surface was yellowish white and waxy. There seemed to be no definite structure to the formation, and he looked upon it as a secretory product collected in the meshes of a cellular
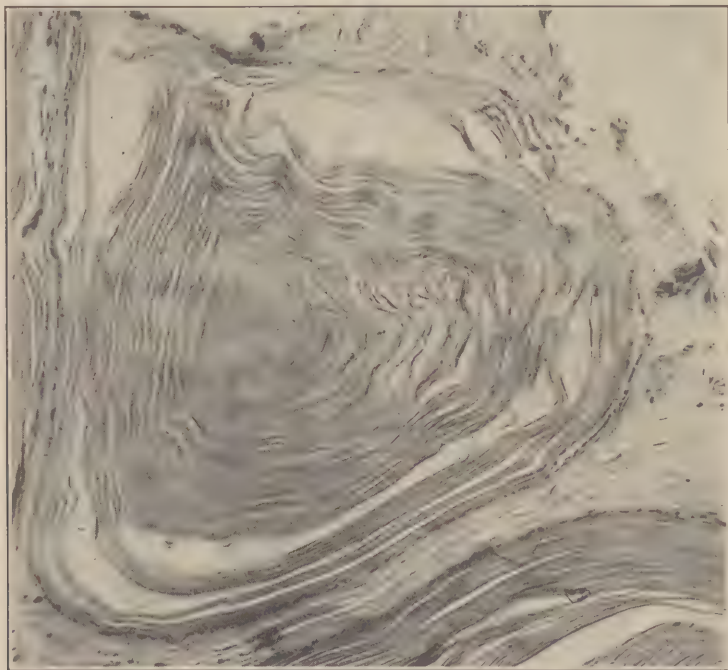
FIG. 50.—Mass of stratified concentrically arranged squamous epithelial cells in a small sebaceous cyst (cholesteatoma (?) of the skin. (*Photomicrograph of Dr. F. D. Weidman.*)

tissue and gave it the name "*tumeur perlée*." He was able to collect several other cases of much the same character, that is, composed of solid or laminated masses of waxy material, without definite intermediate structure.

J. Müller, microscopically examined eight such "laminated fatty tumors" and it is to him that we are indebted for the name "cholesteatoma." The dull mother-of-pearl lustre he attributed to the reflection of the light by the finely concentric layers of the mass.

The microscopic structure he found to consist of delicate polyhedral cells arranged in concentric lamina between which crystalline fat was deposited. The cells were mutually compressed, pale, clear, and anuclear.

Of a total of 15 cases that Müller was able to collect, 6 occurred in the brain, 3 in and about the bones, 2 on ulcers, 1 between the uterus and rectum, and the remainder were cysts. As he found the cholesteatomata of the brain and occipital bone inclosed in a delicate membrane, he called them *cholesteatoma*

cystica to separate them from those found by Dupuytren in a urinary fistula, and by himself in an ulcerated mammary carcinoma.

Virchow reviewed the literature with care, and found that confusion had arisen through the inclusion, in the group, of any or all circumscribed collections of compactly or loosely arranged cholesterin accumulations, and of occasional laminated epithelial formations such as the "pearly bodies" of squamous cell carcinoma. Returning to the primary microscopical studies of Müller as the criterion for correct classification, he concluded that the cellular structure was fundamental, and that the *true cholesteatoma arose through multiplication and concentric lamination of epithelial cells.*

This seems to be the wisest view to take. Sebaceous and other fatty matter in cysts—sebaceous cysts etc.—may, become crystalline and contain large quantities of cholesterin, but are not tumors, and the presence of the crystals is a mere incident by which a pearly lustre is given to the contents. To those accustomed to look upon the cholesterin as the characteristic and diagnostic feature, it may come as a surprise that Virchow looked upon it as entirely subordinate. The essential feature is the cellular structure—the concentrically laminated flattened epithelial cells—the plates of cholesterin between which are usual but not necessary.

As cholesteatoma is treated in the text-books of today, it is difficult to escape the impression that statements have been transcribed from book to book with little thought on the part of the writers, until they have become confused.

Cholesteatoma is first of all a tumor, and as such must be composed fundamentally of tissue. Pearly accumulations, partly or entirely composed of cholesterin, occurring in cysts, old abscesses, ulcers, etc., are ruled out from further consideration. Cholesterin is also commonly present in the contents of wens, dermoid cysts, and atheromatous cysts in the walls of blood vessels, and may occur in almost solid masses. But these are not cholesteatoma, though there may be a closer connection between them and cholesteatoma than at first appears. Ribbert, in his Text-book of Pathology, figures a cholesteatoma of the base of the brain. It appears to be a kind of cyst surrounded by a thin wall of epithelium and distended with an accumulation of concentrically arranged desquamated epithelial cells between which are cholesterin plates. It would seem to be a dermoid cyst primarily, yet it meets the requirements of cholesteatoma, for it is largely made up of the concentrically arranged epithelium with the cholesterin plates between. If this dermoid be a cholesteatoma, why may not any dermoid be similarly so considered, if with its desquamated cells cholesterin be mixed? If so, why not a wen? Indeed Sir James Y. Paget, in his "Surgical Pathology," 1865, discusses cholesteatoma with the dermoids and wens, though he inclines to Virchow's opinion that care should be taken to "distinguish the true cholesteatoma of Müller from mere collections of cholesterin crystals in cysts, dried up abscesses, surfaces of ulcers, etc." Moreover, it is now pretty generally conceded that the cholesteatoma of the meninges, which is the most frequent form, is a teratoblastoma, and arises through the inclusion of ectodermal cells, in the pia, during the development of the nervous system. Ectodermal cells, thus sequestered, may as will shortly be found, give

rise to dermoid cysts, and make the relationship between them and cholestea-tomas very close.

Being then, first of all a tumor and therefore composed fundamentally of tissue, and this tissue of concentrically arranged lamina of flattened cells of polyhedral form, what can be the origin of these cells?

Virchow believed that they arose through metaplasia of the connective tissue, even though he recognized them as epithelial. Böstroem, in a elaborate
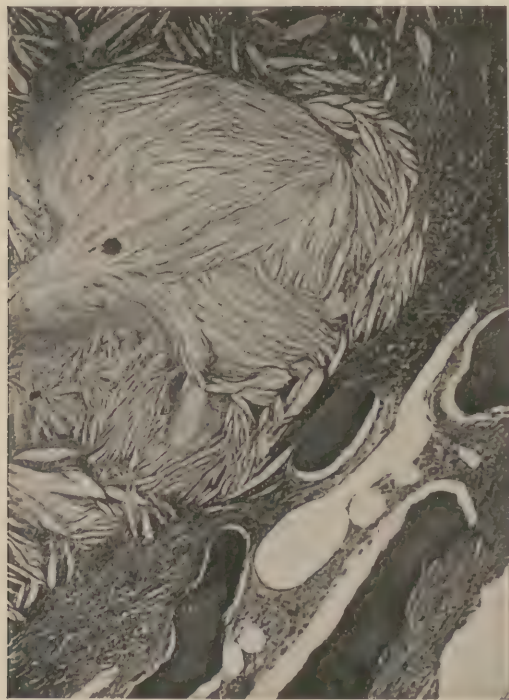

FIG. 51.—Fat crystals in a dermoid of skin. (*Ewing.*)

study of the subject, came to the conclusion that all pial cholesteatomas arose from embryonal inclusions of the epiderm, and that the cells were therefore epithelial and epidermal. In this he was supported by Ziegler who showed that such tumors not infrequently contained lanugo hairs. Glaeser, Frank and others regarded the cells as endothelial, but there seems no longer to be any sympathy with this view.

But, if masses of concentrically arranged epithelial cells occur under condi-tions identical with cholesteatoma, yet have no cholesterin between or among them, will they also be cholesteatomas? According to the conception of Virchow, they will. Then how about similar concentrically laminated epithelial cellular masses in other locations? Will an epithelial peal of squamous cell carcinoma be cholesteatoma? This is obviously going too far. Such epithelial pearls form structural components of tumors whose regular development occurs along different lines from that followed by the cholesteatoma, and makes it

almost impossible that confusion should occur. Yet there is a certain relationship between all of these structures, as is shown by what occasionally happens in the pia, where the epithelial laminations do not always give rise to large concentric bodies with the pearly lustre, but sometimes to congeries of small ones strikingly like the epithelial pearls, but as independent of one another, and of the surrounding atypical embryonal tissue, as are the large lustrous bodies of the well recognized cholesteatomas. Such small aggregated bodies may or may not contain cholesterin, though undoubtedly of the same origin as the large ones. Tumors of this composition are therefore undoubtedly to be included among the true cholesteatomas. Histologically they bear enough resemblance to certain of the dural endotheliomas to permit of a certain amount of confusion, when the cells are not well preserved.

It thus becomes evident that cholesteatoma is not a definite type of tumor but an appearance to be found in various tumors or cysts, or wherever the proliferation of squamous epithelium, or other flat cells, forms laminated masses, that usually, but not necessarily become infiltrated with cholesterin.

The term cholesteatoma is also applied to some morbid formations in no way related to tumors. This is exemplified by the cholesteatoma of the ear. Embryonal inclusions of epidermal cells attending the closure of the first visceral furrow, is followed by desquamation and massive accumulation of the cells which become compressed into concentric masses, and later infiltrated with cholesterin. In these cases there is a kind of concrement—a brittle chalky mass—but no tumor.

More rarely the calyces of the kidney become the points of accumulation of hyperplastic and desquamated epithelial cells of the pelvis which may similarly amalgamate into concentric masses and into which cholesterin later infiltrates.

In addition to these must be mentioned certain cholesterin infiltrations that sometimes make their appearance at the base of the brain, in the mamma, the testis, and elsewhere, and give rise to shining bodies or pearly masses that also receive the name cholesteatoma.

These are usually residual inflammatory and hemorrhagic accumulations infiltrated with cholesterin and fatty acids, and are neither new growths nor tumors. They have no structure, no cellular origin or foundation, and are no more cholesteatomas than the similarly crystallinized fatty contents of wens or dermoid cysts. But when they occur in connection with the membranes of the brain they should be carefully examined microscopically to see that they are not examples of the tumor under consideration.

This analysis shows that there are three entirely different things to which the term cholesteatoma may be applied with justification, though only the first is a tumor.

1. *Cholesteatoma of the Pia Mater*.—This forms a tumor varying in size from a pea to a hen's egg. It usually has a pale color, and may have the typical pearly lustre on the outside, or may show pearly areas upon section, according to the presence of a single or numerous concentric cellular masses. It occurs at the base of the brain, or near one of its great fissures. In more rare instances it may occur in the spinal canal.

It is slow growing, is perfectly benign, but through its position may cause absorption and compression of the subjacent nervous tissue. Occasional concentric cellular masses hyalinize and calcify, and such tumors connect with psammoma.

2. *Cholesteatoma of the Middle Ear.*—Here the desquamated squamous cells transformed into horny shining scales are compressed into a concentrically laminated mass, between which cholesterin infiltrates. It is not until the mass thus formed becomes of considerable size that it attracts attention. Those described in the literature varied in size from a millet seed to a pigeon's egg. They may erode the tympanic membrane, and then appear in the external auditory meatus. When removed they are white, glistening, firm and brittle. The epithelial cells are usually old horny and without nuclei, so that it may be difficult to identify them. In those we have examined, the cells were mere horny scales without nuclei. But they readily differentiate from the cholesterin plates with which they are mixed when subjected to the influence of alcohol and other cholesterin solvents.

3. *Cholesteatoma of the Pelvis of the Kidney.*—These not only occur in the pelvis, but may be encountered anywhere along the excretory passages from the calyces, where they seem to be most frequent, to the urethra. They result from epithelial accumulations following chronic inflammation, compressed into concentric masses and infiltrated with cholesterin. Not infrequently they are subsequently found to have occurred in association with or been the precursors of true neoplasms of the parts.

It is said that similar formations sometimes occur in the uterus, the gall-bladder and the mamma. So little seems to have been done in the way of studying these as to leave some doubt as to their correct structure and classification.

Mixed Tumors

Where development is complicated, and involves the concrescence of adjacent parts, some of the embryonal material belonging to one structure may become included in the other. How frequently this occurs, there is no way of knowing; nor is it actually proven to occur. But the assumption forms the most satisfactory theory by which to account for the origin of certain peculiar tumors whose structure is unlike the nidus from which they spring, and whose histological detail is remarkably complex.

Upon this theory of "embryonal inclusion," modern French authors now commonly speak of such tumors as "*enclavomas;*" but they are better known as "*Mixed tumors.*"

But it is sometimes difficult to know how mixed the structure of the tumor must be in order that it be assigned to this class. In beginning the discussion of the subject, advantage may accrue from the momentary abandonment of the term "mixed tumor," and the substitution of "enclavoma," for by so doing the conception of "mixture" is subordinated and that of "inclusion" emphasized.

It is then immediately possible to assign to one group, all tumors whose heterologous structure suggests origin from an embryonal inclusion, and a circumscribed collection of adipose tissue in the uterus, evidently descended from included adjacent lipoblasts, becomes an enclavome as much as a complex tumor of the parotid gland containing epithelial, fibrous, chondrous and mucoid tissues, although it is unmixed.

But if there is danger that some mixed tumors may not be recognized because they are not mixed, there is also danger that some others be included that are too mixed. The tumors that contain derivatives of all three blastodermic

layers are *teratomas*, and can scarcely be imagined to result from embryonal inclusion, by the most ardent exponents of the theory, but must be attributed to descent from a totipotential germinal cell or blastomere. These do not belong in the class of mixed tumors. Mixed tumors are *teratoblastomas* and are descended from pluripotent, not from totipotent cells. They contain derivatives of one or two, but never of all three blastodermic layers.

To understand the mixed structure of the tumors it is necessary to recognize the following fundamental facts:

1. The larger the inclusion, and the greater the variety of formative cells it contains, the greater the variety of tissues the tumor derived from it may contain.
2. The earlier the inclusion occurs, the less will be the differentiation of its cells, which may be pluripotent, and the greater the variety of tissues the tumor derived from it may contain.
3. The smaller the inclusion, and the smaller the number of its cells, the more restricted the variety of their descendents until from a single differentiated cell only one kind of tissue can descend.

The clinical disposition of mixed tumors is uncertain, and varies according to their descent and structure. Early inclusion of undifferentiated (pleuripotent) cells suggests greater capacity for malignant manifestation than later inclusion of more differentiated (unipotent) cells. Tumors of the former are sometimes highly malignant, those of the latter often benign. But no fixed rule can be made. Some of the tumors destroy life in infancy, some do not appear for many years, then grow slowly, either to do nothing important, or later to take on rapid growth and malignant qualities.

Malignant disposition seems to depend upon the rapid multiplication of embryonal cells, and in thought connects these tumors with the sarcomas, with which they have frequently been confused in the past. But if it involve epithelial tissues, it suggests relationship with carcinoma. In neither case is the error a bad one.

Mixed Tumors of the Mammary Gland

These tumors are supposed to be the result of the inclusion in the tissues of the mammary gland of substance derived from the sclerotomes and myotomes of the developing chest walls.

They are rarely recognized as mixed tumors, and appear in the literature as chondroma, giant cell sarcoma, myxoma, adeno-sarcoma, adeno-lipoma, etc. Some two dozen cases have been recorded, but usually with too little detail to enable a critical study to be made. Almost without exception they have been described as slow-growing, rounded or nodular, encapsulated tumors and there is no evidence at hand to show that any was malignant. With a single exception they occurred in women.

Mixed Tumors of the Ovary

Especial care must be taken in diagnosing a mixed-tumor of the ovary because of the frequency of ovarian teratoma.

Mixed tumors of the ovary are usually called sarcoma, and one is surprised to find how many chondro-sarcomas, osteo-sarcomas, myxo-sarcomas and giant cell sarcomas are said to occur in this situation. A certain amount of suspicion should be bestowed upon all cases in which there is peculiar structure, or composit character.

Embryonal inclusions of the mesenchyme in the ovary date back to the time when the Wolffian body, from which the ovary develops, was itself being perfected. It is therefore but natural that the cells should be pluripotent.

Mixed Tumors of the Palate

According to Lenormant, these, though very rare, are the most frequent tumors of the palate. They occur between the 20th and 60th years of age, and were found by Eisenmerger, who collected 76 cases, to be about equally distributed between the sexes—37 in males and 39 in females.

The tumors usually occur on the velum, at the junction of the hard and soft palate, appearing as single, rounded, encapsulated, laterally situated masses made prominent by the contraction of the soft palate, and sometimes attaining to the size of a hen's egg. When palpated they are rather hard and movable. They do not invade the bones, and are rarely anchored to them, though they may become attached to the tissues of the pterygomaxillary fossa, or to those of the parotid region. They grow very slowly, for years, sometimes as long as 40 years, and usually come to the surgeon with the history of long existence followed by sudden recent enlargement. Their position makes it impossible for them to attain a large size before they cause so much discomfort as to necessitate removal, which probably explains why they are usually said to be benign.
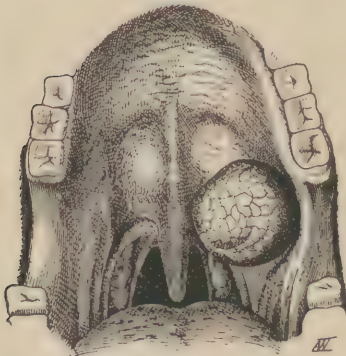
FIG. 52.—Mixed tumor of the palate.
(*Berger.*)

Mixed Tumors of the Pharynx and Tonsil

These have, for the most part, been described as dermoids on account of the covering of lanugo hairs on the external surface. They are rare and interesting formations, of polypoid and solid character, and really ought not be confounded with the cysts. They were described as dermoid polypi by Decleux. Lannelongue and Menard studied them in 1891. Up to 1914 only 35 cases had appeared in the literature.

Growth is very slow, and attention is rarely called to the presence of the tumor until after puberty. Most of the reported cases were in patients between 13 and 22 years of age.

Mixed Tumors of the Lips and Cheeks

Lenormant, Rubens-Duval and Cottard collected 24 cases of mixed tumors of the lips, and 10 cases of similar tumors of the cheeks. According to the

authors mentioned and to Okinczyc who reviewed the cases, all were enclavo-mas. They were small tumors, sometimes solid, sometimes cystic, and had the usual varied structure, in which cartilage and bone were common. Nearly all occurred in the mouths of young persons, and were sub-mucous. They grew very slowly, and in no case is it stated that they showed a malignant disposition.

FIG. 53.—Mixed tumor of the upper lip of 19 years duration. (*New.*)

Mixed Tumors of the Pituitary

These are so rare that not a great deal can be said about them that may not be subject to later revision. Few have been observed, and differences of opinion as to their nature have been expressed. Some have been cystic, and assigned to the group of dermoid cysts, some have shown such complex structure as to seem to fall in with the teratomas. A few encapsulated nodes seem to have been undoubted mixed tumors.

Erdheim found that the stalk of the pituitary occasionally contained small collections of squamous epithelial cells from which tumors might begin or which might serve to add to their mixed character.

6

Mixed Tumors of the Kidney

The kidneys begin development as caecal diverticulae from the dorsal surfaces of the Wolffian ducts, which lengthen and ascend toward the lumbar region. Each of these tubular structures is destined to become the ureter of a future kidney, and soon becomes surrounded by a cellular blastema derived from the terminal portions of the Wolffian ridges. Each such mass of undiffer-

FIG. 54.—Microscopic section of a mixed tumor of the kidney, showing a calcifying and ossifying mass of cartilage, adjacent fibrillar and myxoid tissues, and nondescript epithelial areas in the opposite diagonal corners. (*Photomicrograph by Dr. F. D. Weidman.*)

entiated tissue is carried upward by its future duct which it covers much like a cap. Being in close relationship with the mesonephros or Wolffian body behind, and the sclerotomes and myotomes of the future abdominal wall, it is not remarkable that portions of the latter may occasionally become included in its substance. Presumably it is from such dislocated substance, with or without the addition of surviving vestiges of the Wolffian bodies that the tumors arise. Such possible double origin makes it impossible to scientifically classify these tumors according to the system here adopted. Fortunately, however, that is of not practically importance. The tumors are "mixed tumors," and the

source of the mixture makes very little matter. The connective tissue can be referred to the sclerotomes and myotomes, the epithelium to the vestiges of the Wolffian body, or the organic blastema.

Scientific study of the neoplasms is complicated by their rarity which makes it difficult for any one observer to accumulate enough for satisfactory analysis, and the cases reported by others are difficult to assemble. To find them the reported cases of fibromas, lipomas, myomas, rhabdomyomas, chondromas, myxomas, sarcomas, myxo-sarcomas, adenomas, adeno-sarcomas, carcinomas, hypernephromas, mixed tumors and teratomas must be looked through. As striated muscle commonly forms a conspicuous histological element, the name most frequently applied to them by the older pathologists was *rhabdomyoma*.

These tumors are, of course, congenital. They may begin to grow during intrauterine life, and may be quite large at the time of birth. Appearance may, on the other hand, be delayed until later in childhood or until adult life. The tumors of childhood are usually of rapid growth, effect great destruction, and are fatal, as a rule. Small, apparently inactive lesions of this kind are sometimes unexpectedly discovered, at autopsy, in the bodies of those dead of other causes.

Mixed tumors of the kidneys seem to occur with equal frequency in the two sexes. J. L. Sweet analyzed 100 cases and found 49 in females and 51 in males.

The gross appearance varies according to the structure. If they are formed of fairly well developed elements, they are usually small, well circumscribed and encapsulated; if of embryonal elements, they may be large and indefinitely outlined and even infiltrating. They are usually in the renal capsule, but may be in the renal tissue itself. Naturally, if of large size, these boundaries must be surpassed and they may have capsules of their own, independently of the renal capsule. They sometimes project from the surface, of the kidney, sometimes into the pelvis.

They not infrequently attain a large size. Hoisholt and Jenckel have reported tumors measuring 35 and 37 cm. in length, and Heinicke one that weighed 3580 grammes.

They are usually irregularly rounded, and nodular, and may be soft or firm according to their structure. They are sometimes cystic and partly fluctuating. Metastasis may occur in the liver, more rarely in the lung. Infiltrating tumors are usually hemorrhagic, and hematuria may be among the first symptoms.

Mixed tumors occur independently of the presence of a kidney on the affected side. When a confused mass of tissue, somewhat resembling a mixed tumor, takes the place of one kidney, it is best described as a *hamartoma*, or mass of the undeveloped rudiments. This is not a tumor, however, unless some of the components vegetate unnaturally and excessively.

It is impossible to give an adequate description of the histology of tumors so diversified in structure. When simple, they are apt to be mistaken for ordinary blastomas, from which there is, indeed, no way to differentiate them; when complex, they are composed of varying proportions of fibrillar, mucoid, muscular, vascular, chondroid, and other tissues. In cases complicated by Wolffian inclusions, more or less rich epithelial element is added, in regular form suggesting adenoma or hypernephroma, or in irregular form suggesting carcinoma

The most frequent and suggestive element is considerable embryonal cellular tissue that results in their usual assignment to the class sarcoma.

Mixed Tumors of the Salivary Glands

The morbid growths of the salivary glands are divisible into cysts that are very rare, and solid tumors that are fairly common. Although at first seeming to have nothing to do with one another, these may have common beginnings, and both may be considered with advantage under the present heading.

Acquired cysts of the salivary glands very rarely occur through obstruction of the ducts by calculi, cicatricial bands, or other easily appreciated causes. A few of them have been thought to result from the degeneration of the gland tissue itself, an interesting matter to which it will be necessary to revert later.

The congenital cysts of these glands, though still very rare are more frequent, and are among the congenital condition with delayed manifestations. They do not appear either at birth or shortly after, but only after the lapse of years.

The cysts are most frequent in the parotid, sometimes occur in the submaxillaries but almost never in the sub-linguals. They usually make their first appearance during adolescence, or early adult life, as rounded, elastic, slightly movable, resisting swellings. They are indolent, painless, and do not disturb function. When small they are nearly always mistaken for solid tumors, but as they increase in size and begin to fluctuate, show their cystic character.

When dissected out and submitted to microscopic examination, the wall, formed of connective tissue, is found to contain abundant deposits of lymphoid tissue, and to be lined sometimes with columnar, sometimes of stratified squamous epithelial cells. The contents is said, by Petri, to consist of fluid that reacts like saliva.

This varied structure suggests that the cysts are enclavomas, and only differ from the solid tumors in containing a cavity filled with fluid.

Of the solid tumors of the salivary glands the number is small and the variety restricted. Occasional lipomas of the parotid have been reported; adenomas have been observed by Ribbert, Nasse, Lecene, Wagner and a few others; sarcoma and carcinoma have frequently been reported, but most of them are found to have developed from "mixed tumors." With these eliminated only the *mixed tumor* is left, and the question arises whether some of the other, tumors mentioned were not mixed tumors—enclavomas—unrecognized. The importance of this question may grow upon the reader.

Not only are the mixed tumors the most frequent morbid growths of the salivary glands; the salivary glands are also the most frequent seats of mixed tumors.

Like the corresponding cysts, they do not appear at birth, but are first noticed at or shortly after adolescence. They rarely appear before the 10th or after the 30th years of life.

They form rounded, sharply defined, hard, slightly movable, painless and indolent nodes, that may be intra-glandular or para-glandular, centrally or peripherally situated, in the latter case sometimes below the lobule of the ear or the angle of the jaw and seeming to be in the neck. As they grow they

separate themselves from the substance of the gland by a distinct capsule, and sometimes spontaneously enucleate themselves from the gland. If deeply situated, they cause pressure atrophy of the glandular tissue.

Nelaton and Duplay have pointed out that if a stethoscope be placed over one of them and the jaws opened and closed, a friction sound may be heard.
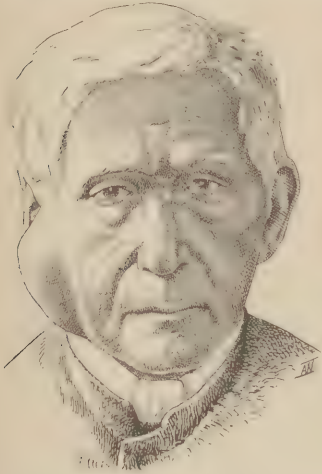
FIG. 55.—Mixed tumor of the parotid. (*Wilms.*)   FIG. 56.—Mixed tumor of the submaxillary gland. (*Kuttner.*)

Mixed tumors of the submaxillary glands, extend upward into the mouth, or downward into the neck. They are so intimately attached that there is usually little difficulty in determining the structure from which they arise as they move readily with the gland, or the gland with the tumor, according to the relative size and importance of the two.

In many cases the tumor requires many years to attain to the size of a nut, and gives the patient no trouble. Such tumors are regarded as benign. But every mixed tumor, and especially those of the salivary glands, must be regarded as potentially malignant, for with the lapse of time conditions commonly change and malignant characters appear. In those cases in which no such malignant change occurs, it may be assumed either that the tumor was benign or that its period of quiescence was so prolonged that the patient had time to grow old or to die of something else before it took place. Pallier observed a case in which the tumor remained inactive for 27 years, and Wood one in which it was so for 50 years. It is not always easy to determine just when the change begins. In some cases the tumor grows slowly and steadily; in others slowly in the beginning, and more rapidly as time passes; in still others it appears suddenly and grows rapidly. Great size may be attained: Morestin observed a parotid tumor that weighed 6000 grammes, Bauchet, one that weighed 3000 grammes.

As the size increases the physical characteristics also change. The growth becomes nodular, and its uniform hardness gives place to alternating hard and soft portions, bespeaking the occurrence of cystic degeneration of its substance.

The general course of the enlargement is usually outward, with the formation of a mass by which the lobule of the ear may be drawn out of shape, and

the external auditory meatus compressed. But it may be inward, when the palpating finger may determine its presence through elevation and bosselations on the pharyngeal wall, where it may sometimes, indeed, be visible.

In rare cases, the tumor, having attained to a large size, seems to rest, and shows no further change; but in most cases the increase in size, especially if rapid, indicates malignancy. F. C. Wood states that 25 % of the tumors becomes malignant. The tumor then slowly but persistently and destructively infiltrates the neighboring structures. If removed it returns, and not more than 20 % of the cases operated upon recover. Metastasis to the lymph nodes of the neck come late if at all. Patients rarely live ten years
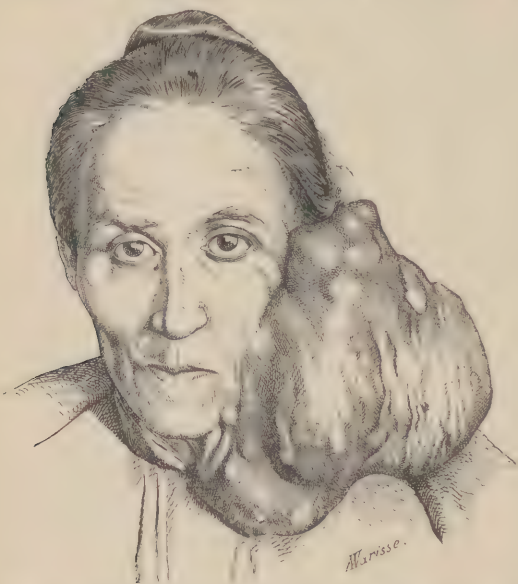
FIG. 57.—Mixed tumor of the parotid in the malignant stage. (*Poncet.*)

from the time active growth begins.

Microscopic study of these tumors reveals a histological structure that has led to many controversies.

Nearly all are composed of epithelial and connective tissues.

Taking the epithelium first, it will be found to differ in appearance and arrangement in different tumors, and in different parts of the same tumor. Sometimes it is definitely squamous, and may form "pearly bodies;" sometimes it is definitely columnar and arranged in glandular alveoli. Some of the cells are nondescript and indefinite an arrangement, leaving one in doubt as to what they really are.

Those by whom the tumors were first studied seemed to have no doubt about the epithelial nature of the cells, and unhesitatingly assigned the malignant members of the carcinoma group. But later came the theory introduced by Wartmann, ardently supported by Volkmann and still cling to in spite of strong evidence to the contrary by Borst and Kaufmann that the cells are endothelium.

Presumably different appearances in different tumors are responsible for these different opinions. But, in some tumors studied by Hinsberg, there were epithelial pearls, the outer cells of which were definitely acanthoid, i.e., spinous, or connected by delicate protoplasmic connections, as are the cells of the middle layers of the epiderm. Similar cells were observed by Wilms and Landsteiner, and the epithelial character of these cells was accepted by Wood and Verhoef. There seems therefore, to be no doubt about the squamous cells, and if they are

epiblastic and epithelial, why should any one seek to prove that the more colum-
nar and cuboidal cells are endothelial?

French pathologists have steadily declined to accept an endothelial origin
for cells so obviously epithelial.

The connective tissue elements are as interesting as the others. The almost
universally accepted criterion for the recognition of the mixed tumor is the
presence of cartilage. When present it makes the identification of the tumors

Fig. 58.—Mixed tumor of the parotid. The tumor, including the fluid in the cysts weighed
3.5 kg. It was removed and the patient recovered. A, Large bone, upon the lower margin of
which were two points of softening; B, softened (necrotic) areas overlying cystic spaces.
(Keen.)

easy, but it may be absent. When present, it sometimes occurs in the form
of well circumscribed scattered islets, of well developed hyaline cartilage; some-
times as highly cellular embryonal cartilage blending with the surrounding less
differentiated fibrillar tissues. The bulk of the tumor may be composed of
mucoid tissue, or of spindle cell tissue with well formed or imperfectly formed
blood-vessels. The proportions of epiblastic and mesoblastic components,
and of the different mesoblastic components vary greatly in different tumors
and in different parts of the same tumor. There is no uniformity of structure.

Granting the correctness of the theory that the tumor descends from a
primodium consisting of included embryonal elements, probably derived from
a branchial arch and adjacent furrows, and that its growth results from the
unequal proliferation of those elements, some of which mature fairly well, while
others remain embryonal, it seems like a waste of time to attempt more than to
regard the tumor as a confused mass of tissue derived from an accidental mix-
ture of embryonal endoderm, ectoderm, and mesoderm. The history of the
tumor seems to indicate that the connective tissue elements grow most rapidly

in the early period, and the epithelial elements, in the later period.   No possible good can come of attempts to classify these tumors as sarcomas or carcinomas. Regardless of the sarcoma-like histological structure they do not behave clinically like sarcomas—do not metastasize through the blood —nor do they regularly invade the lymph-nodes in the manner characteristic of carcinoma.
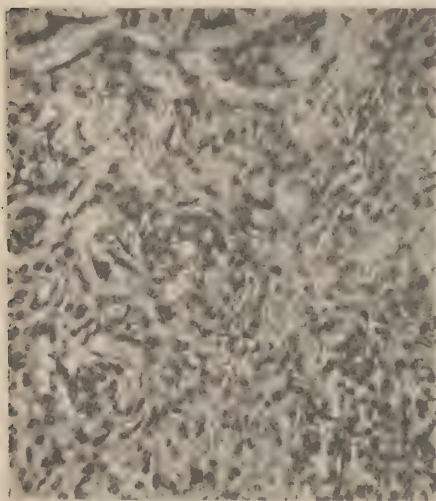
FIG. 59.—Mixed tumor of parotid: Dense fibrous tumor.   (*Wilson and Willis.*)
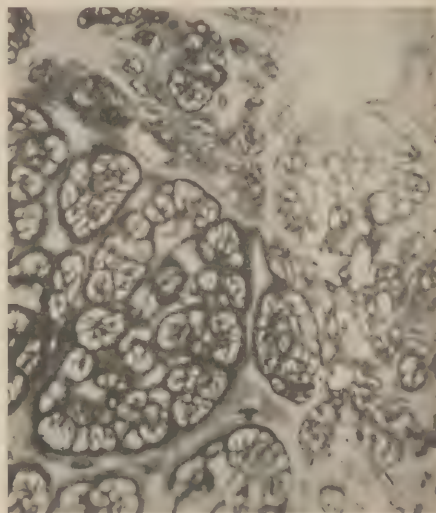
FIG. 60.—Mixed tumor of the parotid: Area showing cartilage.   (*Wilson and Willis.*)

Wilms looks upon the tumors as the result of the inclusion in the parotid gland, of embryonal glandular buds.   The buds being of ectodermal material, can give rise to either squamous or glandular epithelium, both of which he finds present.   The mesodermic elements in the inclusion, can, by differentiation, form the various kinds of connective tissue discovered.

Forgue looks upon them as branchiomas.   Between these two opinions there is no other difference than that having to do with the actual source of the included material.

Forgue sums up the advantages of the branchiogenic over the older theories of epithelial and endothelial origin, as follows:

1. It explains the polymorphism of the tumor.
2. It explains the occurrence of the tumor in a region of complicated development.
3. It explains the independence of the tumor from the parotid gland in which it occurs.
4. It explains the frequent presence of cartilage.
5. It explains the clinical and anatomical identity of the tumors of the parotid and submaxillary glands.
6. It explains the slow and late malignant transformation, which is like that of the branchiogenic carcinoma.

There is no doubt about the propriety of the operative removal of all of these tumors.   The single question centers about the time the operation should be performed.   If the painless small growth is not disfiguring, it may be difficult to convince the patient of the necessity of operation, and, indeed, at that time

removal is not really necessary; but if the tumor begins to grow, no time should be lost, for the tumors are most easily enucleated when small, and at that time are less apt to be in such close relation to the facial nerve as to make its avoidance difficult and subsequent facial palsy from its injury possible.

Mixed Tumor of the Testis and Ovary

Formed of mesothelial elements collected in close proximity to the Wolffian body, some of whose substance, in modified form, enters into the composition of the testis, the embryonal development of these two organs is highly complicated, and takes place in such manner as to make embryonal inclusion easily possible. How frequently mixed tumors result from these apparently favorable conditions is not known however, for the curious reason that in both the ovary and the testis there are other elements, the germ cells, whose disposition to engage in the formation of composit tumors is marked, and whose resulting tissue masses, teratomas, take precedence over them.

But it should be remembered that mixed tumors are of relatively frequent occurrence, and parthenogenetic development of germinal cells rare.

A tumor of the testis or ovary composed of epithelium more or less regularly arranged and supported by a stroma composed of fibrillar, mucous, chondrous or other formed or embryonal tissues, is not different from any other mixed tumor, and may be regarded as such. But the presence of tissue seeming to be identical with that of the thyroid, the mamma, the salivary glands, the liver, the placenta or the central nervous system, is sufficient to stamp that particular tumor as a teratoma, especially if its chondrous or osseous tissue can be determined to have the morphology of a fetal bone.

The mixed tumors of the testis and ovary run clinical courses paralleling those of the more common mixed tumors of the salivary glands. At first they pass through a long period of inactivity, followed by one of slow enlargement lasting a year or more, after which comes rapid growth during which a large size is attained in a few months. It may be then that the patient suffering from the weight of the tumor, dragging pains, and intestinal neuralgia, is first led to seek surgical advice. But it is then usually too late to effect a cure, for the neoplasm has by that time become definitely malignant as is shown by invasion of the lumbar lymph-nodes. Whether the tumor be removed or not, the secondaries spread to the organs, cachexia develops, and death supervenes in the course of about two years.

Mixed Tumors of the Thyroid Gland

Not many mixed tumors of the thyroid gland have been reported in the literature. However, there do occur occasional chondromas and other heterologous tumors and sarcomas of mixed and composite type—myxo-sarcoma, chondro-sarcoma, giant-cell sarcoma, osteo-sarcoma, etc.—tumors not infrequently resulting from embryonal inclusion, and seemingly members of the mixed tumor group.

Mixed Tumors of the Uterus, Vagina and Bladder

In the sections of this work describing atresia uteri, atresia vaginae, imperforate anus and hypospadias, the embryonal development of the tissues concerned in the present section was amply explained. The neck of the uterus, the upper part of the vagina, and the trigone of the bladder, are closely approximated structures of very complex formation, embracing numerous embryonal elements of temporary duration and pronounced subsequent modification. It is from them that the mixed tumors of the neighborhood take origin, and with them may be commingled other mesoblastic derivatives from the sclerotomes and myotomes.

Most of the mixed tumors appearing in this situation have been described as sarcomas. But if an analysis of these sarcomas be made, it will be found that they are interesting and remarkable. In the first place, nearly all of the

FIG. 61.—Grape-like sarcoma or sarcoma botryoides vagina in a young infant. The little patient died of urinary obstruction a few weeks after the photograph was made.

reported cases occurred in early childhood, and were fatal in a very short time. In the second place, the greater number have a peculiar and characteristic appearance, that Spiegelberg has described as "grape-like sarcoma" because of the peculiar cystic appearance, and the unusual manner in which the relatively small cysts hang together, or are attached to the base of the tumor by pedicles. The number of cysts and the length of the pedicles, is, however, subject to considerable variation. In some cases the cysts are scarcely in evidence, the tumor being chiefly solid; in others the cysts seem to be the chief thing, and scarcely any solid substance is present. These are called *sarcoma botryoides*.

A few such tumors have been seen in adult life.

The usual first indication of the presence of such a tumor is the discovery of a soft moist cystic mass, appearing like a bunch of grapes or currants, that is projected from the vagina of the infant when it cries. The interval between the respective cysts making up the bunch may be filled by mucus, or by unrecog-

nizable amorphus matter. The mass grows rapidly, and soon there is difficulty with micturition and defecation, and as the neck of the bladder closes, there is dilatation of the ureters, acute hydronephrosis, and death from exhaustion and uremia.

The tumors are rarely metastatic, and the clinical course is not like that of sarcoma.

In the American Journal of the Medical Sciences, April, 1911, the author published "A Statistical Study of 102 Cases of Sarcoma of the Vagina, with a Report of a New Case of the Grape-like Sarcoma of the Vagina of an Infant." In it references to the cases reported up to that time will be found. However, it is not pointed out in that contribution that many, if not most of the tumors there discussed were mixed tumors. They were described as sarcomas by those reporting them, and were discussed as such. Some were composed of spindle cells, some of round cells, some contained giant cells, some were mucoid, and some were very rich in blood vessels. But a few of them contained striated muscle, and cartilage.

We are thus introduced to a group of tumors more diversified in structure than sarcomas usually are, and that usually bring about fatal results without metastasis.

Dermoid Cysts

The dermoid about to be described is known as the *sequestration dermoid*, and is the result of the accidental inclusion of occasional ectodermal cells in the lines of embryonal concrescence.

Three defects may thus arise:

1. The ectoderm may be elevated and spread out over an excess of mesoderm. Such cases are said to be very rare, but may be more frequent than is supposed, as they may be looked upon as of some other nature unless a hairy surface or other unmistakable character betrays them.
2. The ectoderm may be depressed and retained in a pucker, recess or sinus. From such sinuses tufts of hair frequently project.
3. The included ectoderm may be completely surrounded, and gives origin to a closed space, the dermoid cyst.

It is the wall of the dermoid cyst that is the essential structure; the cavity and contents are incidental, and dermoids can be solid tumors.

When a cyst appears in the skin, the question immediately arises whether it is a dermoid cyst or a wen? The former is a congenital malformation, though its appearance may be so long delayed as to give no suggestion of embryonal origin; the latter is acquired and is a simple retention cyst resulting from the accidental closure of the ducts of the glandular appendages of the skin. The two are frequently confused, and it requires considerable and minute examination to differentiate them.

The wen, sebaceous cyst or atheroma, begins its formation through obstruction of the mouths of the sebaceous glands about a hair follicle. As the obstructed glands expand, the hair follicle itself is distended and its sheath flattened out into a sac common to the follicle and sebaceous glands.

The resulting cystic cavity is lined with squamous epithelium, and filled with accumulated sebum mixed with more or less exuded lymph. As the formative activity of the hair follicle is not immediately set aside, a few delicate hairs may be found suspended in the fluid, the discovery of which may lead to the hasty opinion that the cyst is a dermoid.

FIG. 62.—Wens or sebaceous cysts of scalp.
(*McFarland, "Text-book of Pathology."*)

The dermoid cyst, on the other hand has a wall partly, at least, composed of skin—that is, squamous epithelium supported upon a corium with a distinct papillary layer, and provided with typical appendages. It is the discovery of the papillary layer that makes the identification of the dermoid possible in doubtful cases.

In addition to the papillary layer, the appendages in the wall of the dermoid, may be numerous and striking objects. There may be many hair follicles, and resulting large numbers of hairs, sometimes of the delicate lanugo type, sometimes long and coarse, the color always conforming with those upon the head of the individual. There may be great numbers of sebaceous glands, so that large quantities of sebum may be formed. Or, there may be many sweat glands, so that much watery fluid may be added. There being no outlet, these secretions collect in a space and give the dermoid its cystic character.

The contents vary. In some cases they are mostly watery, with buttery flakes, desquamated epithelium and suspended hairs; in others mostly buttery material with occasional drops of water and hairs. In such cases the contents are so plastic as to assist in the identification of the nature of the cyst while it is still beneath the skin or in the tissues.

In rare cases the contents are rolled into little balls of putty-like material. In the large dermoid of the scalp reported by Sir John Bland Sutton there were 3930 round balls composed of epithelial cells and fat.

In some cases the fat of the sebaceous matter undergoes crystalline change, and cholesterin may appear in considerable quantities. Indeed, in some cases the cyst has seemed to be filled with laminated masses of cholesterin, forming an almost solid body with a pearly lustre. It was to such cases that the name cholesteatoma of the skin was formerly and erroneously applied.

In a few cases, and usually when the cysts occurred about the face and neck, occasional teeth have been found growing in the cyst walls, and desquamated teeth in the contents. In extremely rare cases bone has been observed in the walls of sequestration dermoids of the same locality.

But when the structure of cysts occurring in the distribution of the sequestration dermoids is found to be unusually complex, origin through other means

than the simple inclusion of ectoderm should be suspected. Teratoid cysts and tumors may occur anywhere. The discovery of tissues from three blastodermic layers settles the question. Sequestration dermoids never have derivatives from more than two: endodermal derivatives are always absent.

The great line of embryonal concrescence, as pointed out by Sutton, begins immediately behind the occipital protuberance and descends the middle of the back to the coccyx where it turns forward along the perineum, following the

Fig. 63.—Microscopic section of a pilonidal cyst over the sacrum. The oval bodies are sections of hairs. The opening is not shown, but the stratified squamous epithelial lining is distinct. (*From a photomicrograph by Dr. F. D. Weidman.*)

raphae of the scrotum and penis in the male, then ascends the front of the abdominal wall, passing through the umbilicus, up the front of the thorax and neck, to terminate at the middle of the margin of the lower lip. Anywhere along this line dermoids may originate, and near it most of them will be found. But in addition there are other lines of concrescence on and about the face, to which attention was directed in the section devoted to the arrests of facial development.

A few undoubted sequestration dermoids occur where no concrescence takes place, and are difficult to explain. Such have been found at the tip and root of the nose, and upon the forehead and mid-line of the cranium. Lannelongue

believes them to arise from ectodermal elements of the posterior median fissure of the embryo carried forward and downward by the naso-frontal process as it assists in the formation of the face.

Following Sutton's line of concrescence the peculiarities of the dermoids in different regions be pointed out:

Dermoids of the Spinal Region

These are rare, and occur for the most part in the lumbar and sacral regions. When appearing early, and when situated over the sacrum, they may be mistaken for spina bifida. But the late appearance of the dermoid as contrasted with the spina bifida ought to be sufficient to make the diagnosis. Dermoids do not usually attract attention until about the time of puberty when their increasing size causes annoyance.

Near the tip of the coccyx one occasionally observes a tiny deep dimple or pocket, from which may project a tuft of hair. It is called a *pilonidal cyst* or *fistula*, and in some cases may result from ectodermal sequestration analogous to the similar dermoid pockets upon the nose; in others may result from more complex developmental errors, having to do with incomplete closure of the neurenteric canal. As its position varies, sometimes being near the tip of the coccyx, sometimes over the lower part of the sacrum it seems more likely to be the result of ectodermal inclusion than of the neurenteric canal derivation.
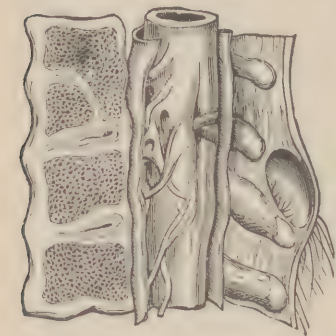
FIG. 64.—Section of three thoracic vertebrae with a small dermoid situated over two stunted spinous processes. (*From Tumors, "Innocent and Malignant," by Sir John Bland-Sutton.*)

In very rare cases a dermoid may be contained within the spinal canal. This means that the displaced cells of the ectoderm caught by the developing bones were turned in instead of out.

This unfortunate accident may result in pressure palsy, the cause of which it may be impossible to discover, even with the aid of the X-rays.

Dermoids of the Vulvar and Scrotal Regions

In both of these regions wens are common and apt to be mistaken for dermoids which are very rare.

When scrotal dermoids are deeply seated and attach themselves to the testis, they easily become confused with teratomas.

Dermoids of the Penis

Congenital cysts have been observed both along the dorsal and ventral surfaces of the penis. The true nature of the former is in considerable doubt. They may be transplanted dermoids, or wens, or some other kind of congenital cysts. But of the occurrence of true dermoids along the raphe there can be no doubt. They are usually single, and situated exactly in the midline, the size

varying from a lentil to an almond. They are usually freely movable beneath the skin, but may be attached to the corpora cavernosa, the glans or the prepuce.

Dermoids of the Groin

In a few cases dermoids have been encountered in the inguinal canal. The inclusions from which they developed are supposed to have been transplanted from the median line.

Dermoids of the Urinary Bladder

It is difficult to account for these as sequestration dermoids; they may have been teratomas. Blick, Bryant, Thompson and Hall have reported cases, and Rayer has shown them to be the source of the peculiar conditions known as *pilimiction* or passage of hairs with the urine.

Dermoids of the Abdominal Wall

These seem to be extremely rare.

Dermoids of the Thoracic Wall

These, also very rare, usually make their appearance in the mid-line of the sternum about the junction of the manubrium and gladiolus. Sutton has pointed out that it is not unusual to discover small cutaneous recesses in this region, and the dermoid is, of course, nothing more than a closed recess.

The most interesting cases occur behind the sternum. These are supposed to have been thrust backward instead of forward by the sclerotomes and myotomes of the developing thoracic wall, and to have reached an appreciable size before the sternum itself was developed.

In this deep position the cysts lose their original relations, and become attached to the pleura, the pericardium, or the lung. Occasionally they arise near the supra-sternal notch, from which they may be forced backward into the thoracic cavity. Lannelongue observed 6 cases, and Lenormant collected 14 cases of cysts of the thoracic wall, 12 of which were dermoids.

Dermoids of the Neck

These may be either centrally or laterally situated, the central ones arising through embryonal concrescence, the others through obliteration of the branchial grooves.

(a) *Median Dermoids of the Neck.*—Dubonnel was able to find only two authentic cases in which the cysts were above the hyoid bone, though Lannelongue has reported eight cases in which they were below. But whether above or below the hyoid bone, the cysts are usually adherent to it. Tachard observed a cyst low down in the neck and adherent to the trachea. Dupres observed one in the supra-sternal notch, and Brocas one so low down that it entered the thorax in front of the trachea and descended to the arch of the aorta. It is doubtful whether these were not thoracic dermoids.

(b) *Lateral Dermoids of the Neck.*—These are still more rare.   In his review of the literature, Lannelongue was able to find only six reported cases, and of these, only one, that reported by Virchow, seemed to be authentic.

FIG. 65.—Dermoid cyst of the neck. (*From a patient in the Philadelphia General Hospital.*)
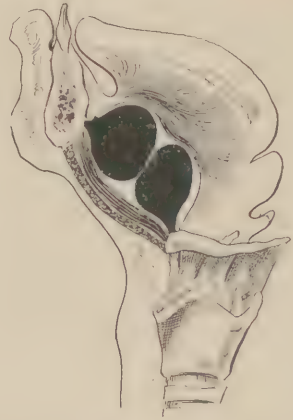
FIG. 66.—Diagram showing how dermoids of the floor of the mouth adhere either to the mandible (adgenian) or to the hyoid bone (adhyoidian).   (*Redrawn from Okinczyc.*)

Dermoids of the Face

These are most frequently situated at the outer end and next most frequently at the inner end of the eye-brow, when they grow to be about the size of a nut

Trans-maxillary fissure

Naso labial fissure

Intermandibular fissure

Cerebral fissure

Intermaxillary fissure
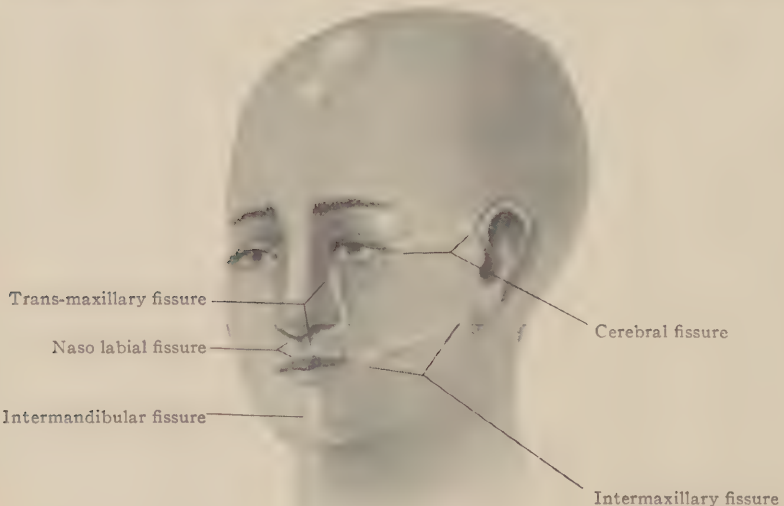
FIG. 67.—Diagram showing the distribution of the sequestration dermoids of the face.   Those upon the scalp have no relation to embryonal fissures.   (*Redrawn from Forgue.*)

or small plum, are fairly firm, and are almost always attached to the adjacent bones.   A few have occurred in the tissues of the eye-lids, unattached to the

bones. One occurred in the orbital cavity and contained a tooth. They have been found as far back as the external ear, and mastoid process.

Dermoids of the nose, to whose unusual position reference has already been made are supposed to result from transplantation of ectoderm by the naso-frontal process, and usually occur either at the tip or at the root of the nose. They are usually quite small, and not infrequently are not cysts, but pockets or sinuses, from which for a bunch of hairs to project.

FIG. 68.—Dermoid fossa on bridge of nose. (*From "Tumors, Innocent and Malignant," by Sir John Bland-Sutton.*)

FIG. 69.—Dermoid fossa on top of nose. (*From "Tumors, Innocent and Malignant," by Sir John Bland-Sutton.*)

Dermoids of the Mouth

These may occur either upon the tongue or palate. Lingual dermoids are supposed to be the result of inclusion of the ectoderm between the halves of the jaw in such manner that the symphysis subsequently forms in front of them. They are usually the size of a nut, but cases have been observed in which the cyst was so large as to project through the permanently open mouth. They are usually embedded in the substance of the tongue, but may be below it, when the organ is thrust upward and its function disturbed.

The dermoids of the palate and pharynx are rarely cystic in character, but rather of the form in which the ectoderm is elevated and spread over an adventitious mass of mesodermal tissue. This results in the dislocated ecto-dermal derivative, skin, accompanied by its various appendages appearing upon the external surface. Decleux called such defects *dermoid polypi*. Some of them without the hairs by which their true nature can be recognized, are unavoidably classed with the mixed tumors.

The tumors usually appear of a pyriform shape, and of the size of the little finger or the thumb, and are attached to the pharyngeal wall, by a slender pedicle, in the immediate vicinity of the Eustachian tube, to the posterior pillar of the fauces, or to a tonsil. Lenormant says "they often hide in one of the grooves of the pharynx in such manner as to escape observation. To find them one may have to resort to touch, or the use of the laryngoscope, or the

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posterior rhinoscope; but touch is indispensible for the discovery of their point of attachment and physical characters. . . . In general they are the size of the little finger or thumb, and consist of a free pyriform extremity attached by a longer or shorter pedicle. They ordinarily hang in the pharynx, but when large, are frequently thrown forward into the mouth, where they appear as a

FIG. 70.—Dermoid at the root of the nose. (*Schaffer*.)

second tongue. In the case of Thelling, the polyp as large as an apple, was constantly outside of the mouth, and accompanied by complete division of the palate. There was also division of the palate in the case reported by Avellis The surface is smooth or shagreen; the mucose, or more correctly the skin which covers them has a blue gray color, darker than the rest of the pharynx, and has many lanugo hairs."

Dermoids of the Scalp

These are also frequently spoken of as dermoids of the cranium because of the peculiar relation they bear to its bones. They always occur in a median position, so that they fall into line with the median cysts of the nose and forehead. The usual points at which they occur are the *gabella*, the suture between the nasal and frontal bones, the *bregma*, the junction of the coronal and sagittal sutures and the *inion*, the junction of the sagittal and lambdoidal sutures.

Cysts of the gabella are rare. Le Dentu saw one and collected six. The median cysts of the forehead are included in this group by some writers.

Cysts of the bregma are a little more frequent; Lannelongue was able to collect 19 from the literature. Some of them attain to a large size. Sir Astley Cooper observed one as large as a coconut that sprang from the vertex of the skull and gave the man a most grotesque appearance "for when he put on his hat, he put it on the tumor, and it scarcely reached his head."

FIG. 71.—Large lingual dermoid protruding from the mouth. (*From "Tumors, Innocent and Malignant," by Sir John Bland-Sutton.*)

FIG. 72.

FIG. 73.

FIG. 72.—Man with a large dermoid of the scalp. (*From "Tumors, Innocent and Malignant," by Sir John Bland-Sutton.*)

FIG. 73.—Intracranial dermoid cyst. The illustration shows a longitudinal section of the cyst and cranial vault. The cyst is filled with sebaceous matter and hairs. A prolongation of the cyst wall blends with the dura mater and penetrates the bone connecting on the outside with a fibrous cord derived from the scalp. The original connection between the cyst and the skin is thus shown. (*Redrawn from Lannelongue.*)

Large dermoids of the bregma and inion may be mistaken for meningoceles as they sometimes rise and fall with the cardiac pulsations, and have been observed to swell when the patient coughed.

Dermoids of the bregma are nearly always *outside* of the cranium, those of the inion *inside*. In a few cases they are partly outside and partly inside. They are always in intimate relation with the bones, and not infrequently seem to lie in a fossa or excavation. More careful investigation, however, shows that the pedicle of an external tumor of this kind, passes through an opening between the bones and connects with the dura mater below, while the pedicles of the tumors that are inside of the skull pass through similar openings to connect with the pericranium on the outside.

This is easily understood. The ectodermal inclusion from which the cyst was derived, naturally took place before the development of the skull, and when the outer layer of ectoderm, that was to form the skin, was in contact with the inner layer, that was to form the dura mater. As the developing bones, beginning below and extending upward to meet in the middle line, separated the layers of primitive tissue, they came into contact with the already existing inclusion, which they displaced outwards or inwards, or about which they grew. If the displacement was outwards, traction was made upon the dural attachment of the defect, which became attenuated into a pedicle; if inwards, upon the pericranial connection which was similarly modified. If the bones could effect displacement neither up nor down, the cyst was surrounded, and a foramen remained.

The relation is precisely the same as in encephalocele, as will be shown later.

The intra-cranial dermoids effect pressure upon the brain, and may so cause death.

Dermoids of the Hypophysis Cerebri

As the pituitary body or hypophysis cerebri is developed partly through exvagination of the posterior pharyngeal wall (Rathke's pouch), and subsequently connects with the structure that is to form its posterior lobe, it is evident that an opportunity for embryonal inclusion is afforded.

Dermoid cysts of the hypophysis are, however, rare. Wilms supposes that they result from the inclusion of fragments of the buccal ectoderm, which seems to be supported by the fact that they sometimes contain teeth. Bonordon observed a case of dermoid of the hypophysis in which there were 14 teeth, as well as thyroid tissue and spaces lined with ciliated epithelium. But the possible occurrence of teratoid tumors must be born in mind when such complex structures are discovered.

Adenoma of the Mammary Gland

Small, movable, rounded, encapsulated, firm tumors are of occasional occurrence in the female breast.

They usually do not make their appearance until after puberty, and then grow very slowly, the patient coming to the surgeon rather because she finds the

curious little body in the breast and is alarmed at the possibility of future trouble resulting from it rather than because she is annoyed by it.

Under Tumors of the Mammary Gland, more will be said about the histological structure of these tumors; at this point their origin is the matter of interest.

The tumors grow very slowly. But if the patient becomes pregnant, and the breasts hypertrophy, the tumor may participate in the enlargement. In some cases it may not seem to increase during pregnancy, but does so later and rapidly as the secretion of milk occurs. This usually means that the tumor has increased its parenchymatous tissue during pregnancy, without increasing its size sufficiently to be noticed, but that with the coming of lactation has taken on function as has the breast itself. The multiplied ducts of the tumor seem to be the source of the secretion, as in the breast of the infant. In rare cases the tumor becomes entirely made up of small structures resembling acini. Such tumors have been from time to time described as *racemose adenomas*, the unusual appearance not being understood.

Now it must be admitted that a tumor in the breast, consisting of tissue different from, but similar to the tissue of the breast, behaving as nearly as possible like the breast under stimuli that affect the breast, is a very peculiar thing. How shall its occurrence be accounted for? The most satisfactory explanation seems to be that which presupposes it to be an embryonal inclusion of primitive mammary tissue in the organ to which it actually belonged, so sequestered that it could not develop as a part of the whole, but became a separated and independent entity.

Fetal Adenoma of the Thyroid Gland

The fetal adenoma is a smaller or larger, rounded, well encapsulated mass of thyroid substance, inclosed within the structure of the thyroid gland. Its histological features correspond with those of the gland. Except that it is without fibrous partitions or trabeculae.

It is now generally admitted that the fetal adenomas of the thyroid are congenital and result from delayed growth of embryonal thyroid cells in the developing thyroid, in such manner that they became sequestered and surrounded by connective tissue.

Hypernephroma

The adrenal bodies make their appearance, in human embryos, about the beginning of the fourth week, independently of any antecedent structures.[1]

At that time the Wolffian bodies are well-formed, and it is in the neighborhood of their inner upper ends that they first appear as proliferations of the coelomic mesothelium dipping into the subjacent mesenchyme. The two distinct masses soon appear, one on each side of the upper portion of the abdominal aorta, and, at first consist entirely of the epithelium, that is later to constitute the cortical portion of the glands. To these the name "*inter-renal masses*" is applied. During the ninth or tenth weeks fatty granules begin to appear in the cells, and during the fourth month chromaffine cells invade their substance from the sympathetic system. Irregular commingling of the two ele-

ments continues for a long time, and the complete differentiation of the organs into cortical and medullary portions may not be effected until after birth.

The interrenal masses are not compact and fragments not infrequently become separated, and subsequently develop independently into what are spoken of as *supernumerary* or *accessory adrenals*. They should not, however, be so called unless the supernumerary body be provided with both cortical and medullary tissues, so as to constitute a real organ. If they consist of the cortical portion only, it would be better to call them *supernumerary inter-renal bodies*.
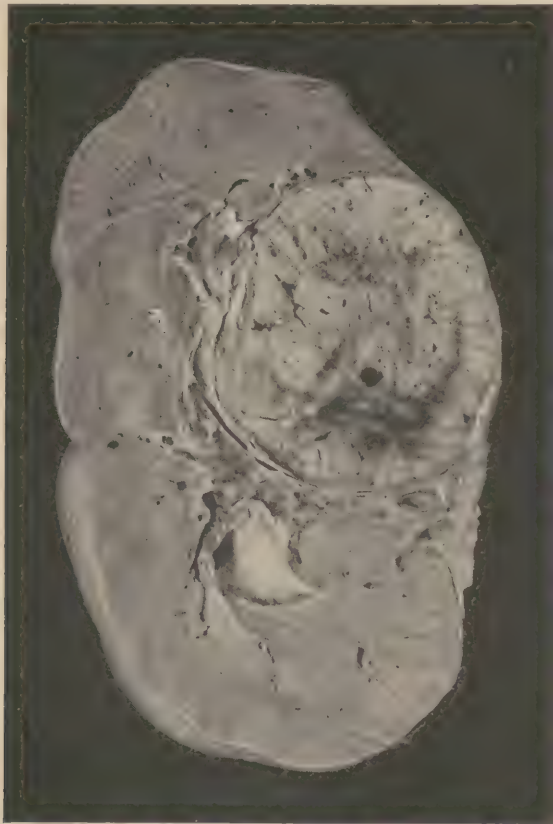
Fig. 74.—An adrenal tumor of the kidney. (*Ewing.*)

They most commonly consist of cortical substance only, vary in size from visibility to a hazel nut and usually lie close to the adrenal bodies, though they may be widely separated from them. They are of frequent occurrence, and Schmorl states that they can be found in 92% of autopsies. The cells of which the supernumerary inter-renal bodies are composed resemble those of the cortical substance of the adrenal, and according to the size of the bodies may be arranged more or less definitely like the zona fasciculata, the zona glomerulosa or more rarely like the zona reticularis.

Ivar Broman supposes them to be formed in either of two ways:

I. Primarily, that is, through failure of all of the adrenal buds to coalesce and form the normal gland.

II. Secondarily, through the detachment of small fragments from the single chief organ.

When not too widely separated, the parts may subsequently unite with the chief organ, and it is by no means uncommon to find small or large masses of cortical structure, included in the cortex, or more rarely in the medulla, of an otherwise well-formed organ.

The occurrence of adrenal tissue too widely removed from the normal adrenals to become united with them, was first pointed out by Marchand, who, in 1883, found one in the broad ligament of the uterus, near the parovarium. They have since been observed in many places, which Broman has tabulated as follows:

1. In the male.
   In the rete testis and epididymis.
   In the paradidymis.
   On the spermatic cord, in the inguinal canal, and above and below the same.
2. In the female.
   In the ovary, where they may easily be mistaken for shrunken corpora lutea.
   On the tubes.
3. In both sexes.
   In the retro-peritoneal tissue below the poles of the kidneys.
   Along the internal spermatic and ovarian veins.
   On the ilio-psoas muscle at the brim of the pelvis.
   At the sacro-iliac synchondrosis.
   In the capsule of the kidney, and in the kidney substance.
   On the wall of the neighboring vessels.
   In the solar and renal sympathetic plexuses.
   Between the transverse colon and the spleen.
   In the right lobe of the liver.
   In the pancreas.

The detached bits of adrenal substance may do any one of three things:
1. Perfect their development as far as possible, then remain unchanged.
2. Retrogress, soften and disappear with the formation of a cyst.
3. Grow lawlessly and form a tumor.

The tumor that thus results is almost universally known as *hypernephroma*, and its most common seat of occurrence is the kidney.

That certain kidney tumors might thus arise was first suggested by Grawitz in 1883, when he described a typical one under the name "*struma aberrata suprarenalis*." His view was soon indorsed by such competent observers as Chiari, Horn, Lubarsch, Benecke, Ambrosius, and Marchand. But in 1893 Sudek opposed the theory, and in his turn was supported by Stoerk, Zehbe, Wilson, Willis, Ipsen, Glynn, and others. A voluminous literature quickly sprang up without throwing much light upon the subject, and after its perusal one finds himself with much the same preconviction with which he began.

In his excellent work upon "Neoplastic Diseases," Ewing concludes,

"That the presence of adrenal rests in the kidney is fully attested, although they are less frequent than many have supposed. It also appears that certain tumors arise from these rests,

although clear description of their structure has not been fully given. Finally, recent studies have demonstrated that a large proportion of the reported hypernephromas are renal adeno-carcinomas."

He seems to be of the opinion that hypernephroma is a somewhat rare tumor, and that the adenoma and adeno-carcinomas of the kidney have little to with it or with adrenal rests.

On the other hand, Garceau, in his book upon "Tumors of the Kidney," inclines toward the opposite view, but wishing to be conservative, says,

FIG. 75.—Hypernephroma. (*Wilson*.)

"It is evident, consequently, that until some definite agreement shall have been decided upon, in regard to tumor classification, we cannot do better than to relegate these growths to a class by themselves. The fact that they develop from adrenal rests in the kidney is now so commonly admitted that there are few who deny it. It seems to be an incontrovertable fact. The best name for the growth, therefore, one which suggests their pathogenesis, is that first proposed by Lubarsch, *hypernephroma*."

The difficulty seems to depend in part upon two seemingly false assumptions with which those who study the subject seem to set out. The first of these is the belief that all tumors must, somehow, certainly fall into one or another of the classically recognized classes of tumors, and therefore have some well recognized name. The second, that if the tumor originated as an adrenal inclusion, it must definitely retain that structure.

When an embryonal tissue fragment is displaced and included in an environment not its own, what follows may depend upon a variety of circumstances, and cannot always be predicted. It depends in part upon the time at which the dislocation occurred; if very early and before differentiation took place, the result may be very different from what would have occurred if it had taken place later and after considerable differentiation had occurred.

An aberrant group of cells destined to form part of the adrenal body, remaining in close relation with the parent mass, and in close relation with other masses entering into the composition of the gland, may develop into an organ difficult to distinguish from the normal organ except by its smaller size, different shape, and supernumerary character. But the same mass more widely separated, and in a position making it impossible for the essential chromaffine cells to find their way into it, might develop into something bearing only a partial

FIG. 76.—Hypernephroma of the left kidney. The rounded mass to the inner side of the hilum of the diseased organ is a metastasis filling the left renal vein and extending into the vena cava. (*Weidman.*)

resemblance to the adrenal, though still recognizable through the size of its cells and their general arrangement in columns. But if the separation be conceived to have taken place still earlier, and the mass been carried a still greater distance from the influences tending toward organic development, the glandular resemblance might be much less pronounced, and it might be with difficulty that the true derivation of the structure is determined. And to complete the

series, it can be imagined that the very earliest segregation, taking place prior to any specific organic differentiation, might result in the development of some structure entirely without resemblance to adrenal, when it might be impossible through its heterologous appearance to discover the origin and nature of the growth. However, if it could be made to fit in with a long series of cases with diminishing organic resemblance, it might be possible to conjecture as to its nature, with a reasonable amount of accuracy.

That aberrant fragments of adrenal tissue occur is indisputable; that hydronephroma develops from them seems to us most reasonable. How else may the tumor be explained?

De Paoli, in 1890, tried to study such of these tumors as came under his observation, with an unprejudiced mind. He noted the resemblance the cells of the tumor bore to the adrenal, and their alveolar arrangement, yet came to the conclusion that the tumors were angio-sarcomas.

Sudek, in 1893, believed that he had traced the development of the tumor from the cells of the uriniferous tubules of the kidney.

Hansemann, in 1902, decided that many of the tumors in question were endotheliomas.

Wilson struck a new note when he suggested that hypernephromas were derived from the mesonephric tubules of the Wolffian body, accidentally included in the developing kidney.

Most writers upon the subject find it necessary to point out the histological resemblance certain parts of the tumor tissue bear to the adrenal. Some writers seem to feel themselves called upon to explain why they adopt an attitude opposed to the apparent facts of the case.

It goes without saying that the inclusion of a bit of aberrant adrenal tissue in the kidney or other organ, does not constitute hypernephroma. That is simply aberrant adrenal tissue or supernumerary inter-renal body. To be hypernephroma the inclusion must grow to be a tumor. It must have surpassed the size possible for an aberrant adrenal. Garceau recognized this, and in compiling his statistics, ruled out all cases in which the body under consideration did not reach a diameter greater than 4 cm.

Apparent increase in size without essential change in the type of structure may result in "benign hypernephroma" not infrequently considered as adenomas. The difficulty in these cases is to decide whether they were originally formed as found at autopsy, or had increased. Their presence was not detected during life.

Some writers seem to consider all adrenal segregations as potentially malignant, and liable to grow into tumors. It would seem as logical to regard the adrenals themselves in the same way.

The inter-renal substance that forms the primordium from which a malignant hypernephroma developed, may never have shown greater resemblance to the adrenal, than is found in the tumor. It may never have reached the stage of organic differentiation.

Malignant hypernephroma is usually characterized by symptoms, of which pain and hemorrhage are the most frequent and most important.

The pain may be the result of pressure upon the lumbar nerves, but when it is associated with hemorrhage, more probably depends upon distension of the renal pelvis with blood clots, or blocking of a ureter.

The hemorrhage, which usually frightens the patient, and may be the symptom that first brings him to the physician, is usually slight in the early stages, when it can be referred to hyperemia of the renal tissue caused by the presence of the tumor, but becomes greater later on when it depends upon the invasion and destruction of the kidney tissue itself.
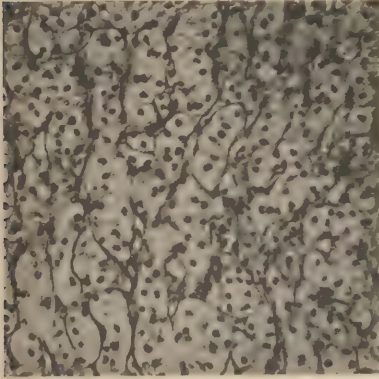
FIG. 77.—"Hypernephroma" cordons. (*Wilson and Willis*.)
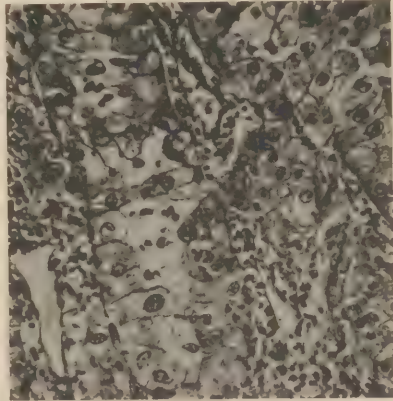
FIG. 78.—Hypernephroma, showing beginning tubule formation. (*Wilson and Willis*.)

The general course of the tumor varies. In some cases it remains a local disturbance, centering in the kidney which is gradually disorganized, while the patient suffers from the repeated hemorrhages, becomes weaker and weaker from loss of blood, and falls into cachexia and dies only after the lapse of years. Cases have been known to live 15 years after symptoms appeared. In other cases the tumor grows rapidly and shows early blood metastasis, followed by the widespread development of secondary tumors and death in a year or two. The metastases of hypernephroma are sometimes remarkably wide spread, and scarcely an organ of the body escapes. Metastasis to the bones is common and may give rise to spontaneous fracture. In the vertebral column the tumor has been known to cause transverse myelitis with paraplegia. Large secondary tumors have been known to obstruct the bowels. Microscopic examination of the secondaries, shows a structure usually repeating that of the primary tumor. Indeed in some cases the diagnosis of the presence of an undiscovered hypernephroma has been made through the microscopic examination of a nodule removed from the surface of the body under the misapprehension that it was a primary tumor.

A rare cause of death is the extension of the tumor to the heart by invasion of the veins.

The delay in the manifestation of malignancy is supposed to depend upon encapsulation of the tumor. Before local invasive destruction of the kidney can

occur, the capsule must be ruptured or disorganized, and before metastasis can occur, intimate connection with the veins must be established, both of which conditions require time.

It has been suggested that if the tumors arose from adrenal substance, they should contain adrenal products, the presence of which should be demonstrable through chemical examination of the tumor or by symptoms manifested by the patient.

This does not seem to be a valid argument. The structure represented in the tumor is cortical, and it will be remembered that the cortical substance of the adrenal is the source of a secretion whose excess or diminution is followed by no characteristic sign. Adrenalin occurs only in the medulla which rarely appears in the tumor. If the same test were required to prove the true nature of the fetal adenoma of the thyroid, it would often fail. But with regard to adrenalin, the matter has been investigated from both points of view, without success. Keen, Pfahler, Ochsner, and others studied the blood pressure, which seemed to be elevated; others failed to confirm the findings. Croftan extracted from a hypernephroma something that destroyed the blue color of the starch reaction, and transformed starch into dextrine. He therefore thought that he found adrenalin. Others found the reaction inconstant, and Ellis found that other extracts would react similarly.

There is less difficulty in recognizing the hypernephroma than in agreeing upon its origin. It ought be easily diagnosed, as it usually has distinctive qualities both to the naked eye and to the microscope. The following are the essential features as first pointed out by Grawitz:

1. Its location under the capsule of the kidney, where adrenal inclusions occur.
2. The sharp encapsulation by which the tumor is separated from the renal parenchyma.
3. The resemblance that the structure bears to that of the adrenal.
4. The presence in the smaller tumors of a fibrous core and more glandular cortex.
5. The character of the cells which differ markedly from the renal epithelium in their high content of fat without signs of degeneration.

Though more frequent in the kidney than in any other organ hypernephroma is not confined to it, but may occur in any of the organs in which adrenal fragments are known to occur—another argument in favor of its adrenal origin.

Aberrant Pancreatic Tissue

The buds from the duodenum and lower part of the bile ducts, from which the pancreas is to develop, gradually become divided and subdivided until the characteristic lobulated structure is reached. But as the organ is thus forming, fragments sometimes become separated from the main mass, and later appear in the form of accessory or supernumerary pancreati, or bits of pancreatic tissue included in other organs or tissues. Klob seems to have been the first to call attention to them, and Leydig showed them to be but modifications of what normally takes place in certain of the lower animals. The mole, for example, always has pancreatic lobules widely removed from the main organ; certain frogs, such as Pelobates, regularly have parts of the pancreas in the wall of the stomach, and certain salamanders always have them in the wall of the duodenum.

In 1904, Warthin made a survey of the literature, and collected 49 cases of aberrant pancreatic tissue. In 1913, Weidman again reviewed the literature, and added 19 more. In some of the reported cases there were several different aberrant fragments, so that altogether there are about 72 occurrences on record. 68 were in relation with the stomach or intestine; 18 in the wall of the stomach, 35 in the duodenum and jejunum, 3 in the wall of the ileum, 6 in diverticulae, and 4 in Meckel's diverticulum. One fragment was in the mesenteric fat, and one was in the great omentum. Most interesting were the remaining cases in which they were in the capsule or in the hilum of the spleen.

In the case reported by Weidman, numerous lobules of pancreatic tissue were scattered over a wide area in the capsule of the spleen.

Most of the larger aberrant pancreatic fragments are typical in structure, and show both the pancreatic lobules and bodies of Langerhans. In 18 of the

FIG. 79.—Hypernephroma of the kidney, showing advanced tubule formation. (*Wilson and Willis.*)

reported cases bodies of Langerhans were found. In nearly all cases there were ducts that presumably had some connection with the alimentary canal, as cystic dilatations were never mentioned.

Zenker assumed that for each supernumerary pancreas there was a separate rudiment. Warthin thought that unnecessary as the developing buds of pancreatic tissue might easily be snared off by the surrounding mesoderm and carried to the abnormal situation in which it was found. Adami supposed this to be possible only after the cells were so far differenitated as to have become unipotential—i.e., capable of producing only one type of tissue.

Weidman accepted Warthin's theory finding that it applied very well in his own case in which the numerous pancreatic fragments were surrounded by connective tissue.

The size of the supernumerary pancreati varies greatly, the smallest on record was 0.4 mm., the largest 9 cm. in diameter. They are usually flattened, and most commonly appear as discs in the alimentary mucosa.

Some think that cancers of the stomach and intestine may originate from these structures, but there is no evidence to support such a view, as in one only of the 72 cases on record, that of Ellis, called adenoma, is mention of malignant disease made, and he thought that in his case he recognized "beginning malignancy."

ABERRANT AND SUPERNUMERARY THYROIDS

In most of the text-books the thyroid gland is described as arising from three separate portions, one central, which becomes the isthmus, and two lateral

which become the lobes.   The central portion is first seen as a little bud or pouch at the apex of the groove between the anterior and posterior portions of the developing tongue, and in embryos of about 3 mm.   As it deepens, its extremity becomes bilobed.   When the embryo has reached a length of about 7 mm., it has entirely separated itself from its origin from the pharynx, but the point of original attachment remains as a depression to which the name *foramen caecum* is given.   The detached rudiment of the gland descends the neck until it reaches its normal situation.   The lateral portions are supposed to arise from the fourth inner visceral pouches, and appear later than the median portion, being first observed in embryos of about 10 mm.
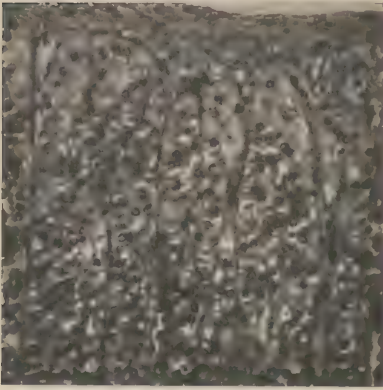
FIG. 80.   FIG. 81.

FIG. 80.—Adrenal cortex. (×200.) Showing cordon formation of adrenal. (*Wilson and Willis.*)
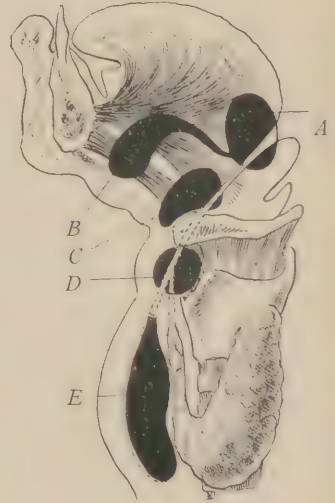
FIG. 81.—Diagram showing the distribution of thyro-glossal vestiges with their cysts and tumors. *A*, Position of lingual thyroid; *B*, position of portion lined with ciliated epithelium; *C*, supra-hyoidian cyst; *D*, sub-hyoidian cyst; *E*, median cyst of the neck. (*Redrawn from Okinczyc.*)

At the present time there is a tendency to regard the central portion as the sole source of the gland.   It is thought that the bilobed rudiment migrates down the neck, becoming a transversly elongated body as it does so, and thus becomes the entire gland, from which, somewhat later, in embryos of 2.6 cm. an outgrowth somewhat to the left of the middle line ascends the neck to form what is known as the pyramid of the organ.   The thyroid gland is thus more and more looked upon as an end organ of the thyro-lingual duct.   In the course of the described migration, vestiges of the primitive gland tissue are sometimes left behind, or carried too far, or are caught by other structures and diverted to abnormal positions, in which they later develop into aberrant or supernumerary thyroids, which most frequently lie in close relation with the organ proper, appearing as lobulations upon its surface, but may be partly or completely detached from it.   Thus, they sometimes lie behind and below the parent organ,

sometimes as far away as the aortic arch or sub-sternal region; or, they may lie higher up, in the trachea, larynx, at the base of the tongue, or at the orifice of the internal auditory meatus.

But the occasional occurrence of supernumerary thyroids in the sides of the neck, makes it probable that the older view of the embryogenesis of the gland is correct, and that some of its substance is derived from the branchial grooves. About 20 cases of lateral cervical thyroid collections have been reported.

Fig. 82.—Lingual thyroid seen in cross-section.   (*C. H. Mayo.*)

How frequent aberrant collections of thyroid substance really are, is difficult to say as they commonly remain undiscovered, unless pathological change affects them.   It may be because of their unrecognized presence that occasional complete extirpations of the thyroid have not been followed by cachexia strumi priva. After the removal of the gland proper, the accessory tissue carries on its function.

But occasionally, these adventitious structures develop into good-sized glands, may develop into goitres, and as in the instances reported by Hinterstoisser, Gutmann, Pool, Wohl and Greensfelder and Bettman, seem to be the source of malignant tumors.

According to Okinczyc they may be entirely free from connection with the gland proper, or may be attached to it by a pedicle.   He has observed them in the mediastinal, retropharyngeal, lingual, and endotracheal regions.

J. Bland Sutton speaks of them as "occasionally occurring in connection with the germs of the lateral lobes and most commonly found in the neighborhood of the greater cornua of the hyoid bone. They are innocent, but if goitre develop may enlarge greatly. Sometimes they enlarge on their own account, and produce tumors that closely resemble unilateral enlargement of the thyroid and occasionally give rise to bronchoceles of moderate size. A bursa extends between the body of the hyoid and the thyro-hyoid membrane when large, it has been mistaken for a dermoid or an accessory thyroid."

The most frequent and most important of the supernumerary thyroids occurs in the tongue, and is, hence, known as the *lingual thyroid*. It was first described in 1897 by Chamisso and Boncourt, who called it goitre of the tongue, and reported 14 cases. Rethius subsequently collected 32 cases, and still later Lenormant, wrote in his "Précis," that the whole number of reported cases had reached 43. At present about a hundred cases are on record.

Lingual thyroids are the result of the accidental dislocation and sequestration of cells from the rudiments of the thyroid as it descends the neck in the migration already described through the thyro-lingual duct or canal of Bochdalek. It stands in close relation to the cysts of the tongue later to be described, for the displaced cells sometimes lead to solid formations if the canal entirely close, to partly solid and partly cystic ones if the canal be partly open, and to cysts if the canal remain largely open.

Fig. 83. Lingual thyroid. (*C. H. Mayo.*)

Lingual thyroids are almost entirely limited to the female sex. Of 43 published cases, only 3 occurred in males.

They are, of course, present at birth, and Hickman saw a new-born infant smother to death because of a large one. Ordinarily, however, they escape observation until later, and usually do not call attention to themselves until puberty, or sometimes not until pregnancy. Most of the reported cases came under observation between the 16th and 30th years of life.

The tumor is usually seated in the middle line, in front of the epiglottis, at the level of the foramem caecum, more or less deeply embedded in the tissue of the tongue. Gellé and Beirtin have reported one as large as a mandarin orange, but the usual size does not exceed a cherry. The suprajacent mucosa is normal, and movable, but apt to be marked by veins. The tissue is vascular, and bleeds

readily when injured.   In a few cases a second supernumerary structure accompanies the lingual thyroid, and is found below the hyoid bone.   It may be connected with the other by a fibrous cord as in the case been reported by Matti.

The detention of the thyroid substance to form the accessory organs is sometimes at the expense of the gland itself which may then be without its
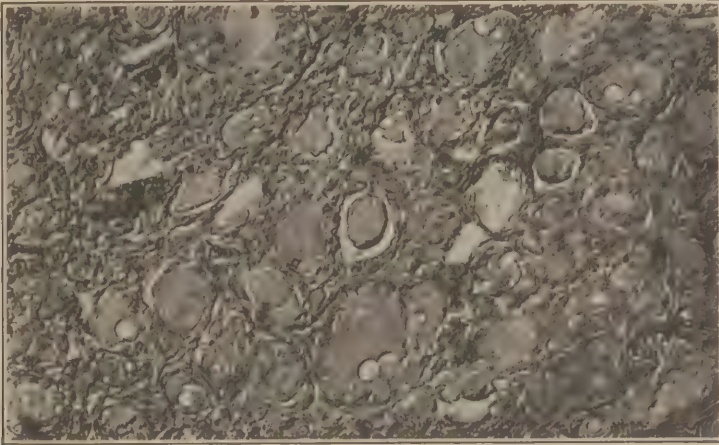
Fig. 84.—Microscopic section of a cervical (branchial?) thyroid.   (*Photomicrograph by Dr. F. D. Weidman.*)

isthmus, and in a few cases there was no other thyroid tissue than that which occurred in the abnormal position.   One of the first and most important things to be remembered when an operation for the removal of a lingual thyroid is contemplated, is to determine that in addition to the abnormally situated structure, there is also a normal one.

Seldawitsch, Chamisso, Rhethius, Lenzi, Berger, Matti, Fereroff, and others have all observed the appearance of myxoedema after the removal of lingual thyroids, because there was no remaining thyroid tissue after the operation.

The presence of lingual thyroids is usually attended by few if any symptoms, but in some cases there is a vague sensation of lump in the throat and slight impediment to deglutition.   If larger, there may be attacks of cough and suffocation.   All of the symptoms will immediately intensify if goitrous enlargement takes place.   Gallé and Bertin were on one occasion compelled to perform tracheotomy on account of impending suffocation from a lingual thyroid.

If a patient present herself with a rounded tumor at the base of the tongue, lingual thyroid should always be suspected, but no operation contemplated unless there is distinct indication for it.

ABERRANT HEPATIC TISSUE

E. Wagner was the first to point out that small masses of hepatic tissue can sometimes be found in the suspensory ligaments of the liver, but since his contribution scarcely any additional observations have been made.

8

Aberrant Splenic Tissue

The spleen makes its first appearance in embryos of about five weeks of age in the form of a thickening and elevation of the mesenchyme and its mesothelial covering, into which at a later period the mesothelial covering cells penetrate. Much later the whole is gradually separated from the surface of the mesogastrium by constriction, until it remains connected with it by a narrow band through which its vessels enter.

In the stage of separation by constriction, irregularities are of frequent occurrence, for in at least 1 per cent. of autopsies small supernumerary spleens are to be found. They are sometimes single, sometimes multiple, and as many as four hundred have been observed in the same individual. They are usually situated in the hilum of the spleen itself, but may be widely separated from it, and are sometimes found embedded in the substance of the pancreas. They vary from visibility to almost one half of the splenic substance in size. The shape is usually round, and the blue-slate color and general appearance are so much like that of the spleen itself that there is usually no difficulty in recognizing them. In one case the author saw one that measured seven by three by one centimetres, was flattened in shape, had a distinct hilum of its own, and lay far from the splenic region, near the head of the pancreas, and not having the usual color, was at first supposed to be a supernumerary liver.

In many cases the gastro-splenic omentum is studied with small bodies of this kind.

Histologically they have the usual splenic structure.

Their surgical importance lies in the fact that the operation of splenectomy might be complicated if in addition to the removal of the spleen itself, a number of supernumerary spleens had to be dealt with.

The palpable presence of a number of rounded bodies associated with splenic enlargement may also give the impression that the abdominal cavity is occupied by tumor masses.

Aberrant Ovarian Tissue

This is rare, and no doubt occurs at the time that the ovary is in the stage of the indifferent sexual gland. The supernumerary ovaries are usually found in close proximity to the normal organs, that is in the broad ligaments. They may be of considerable size, or very small, when they are apt to be overlooked during ovariotomy. They have the typical histological structure of the ovary and are subject to its diseases. If completely disguised through pathological change, the origin of the lesion may be very obscure.

Their presence may also account for the occasional persistence of menstruation and ovulation after ovariotomy.

Aberrant Endometrial Tissue

In rare instances endometrial tissue, or at least, tissue histologically indistinguishable from it, is found in abnormal or ectopic positions. The accom-

panying diagram, taken from Cullen, shows the distribution better than words can express it. How the separation and segregation take place in difficult to understand, except upon the general close approximation of the organs of the early embryo, and the imperfection and looseness of their textures.

Wherever the endometrial tissue occurs, it behaves as in its normal uterine environment, participating in the congestive and exudative phenomena of

Fig. 85.—Various points at which endometrial tissue has been observed by Cullen. 1, In adenomyoma of the body of the uterus; 2, in adenomyoma of the recto-vaginal septum; 3, in adenomyoma of the uterine horn or Fallopian tube; 4, in adenomyoma of the round ligament; 5, in the hilum of the ovary, usually unaccompanied by a myomatous growth; 6, in the utero-ovarian ligament; 7, in the utero-sacral ligament; 8, in the sigmoid flexure; 9, in adenomyoma of the umbilicus. (*Cullen.*)

menstruation. If the resulting accumulation is absorbed, the condition passes unnoticed; if it remains and gradually increases, cysts filled with a dark chocolate like fluid are formed. Should the endometrium behave abnormally, tumors either benign—adeno-myoma—or malignant—adeno-carcinoma—may develop.
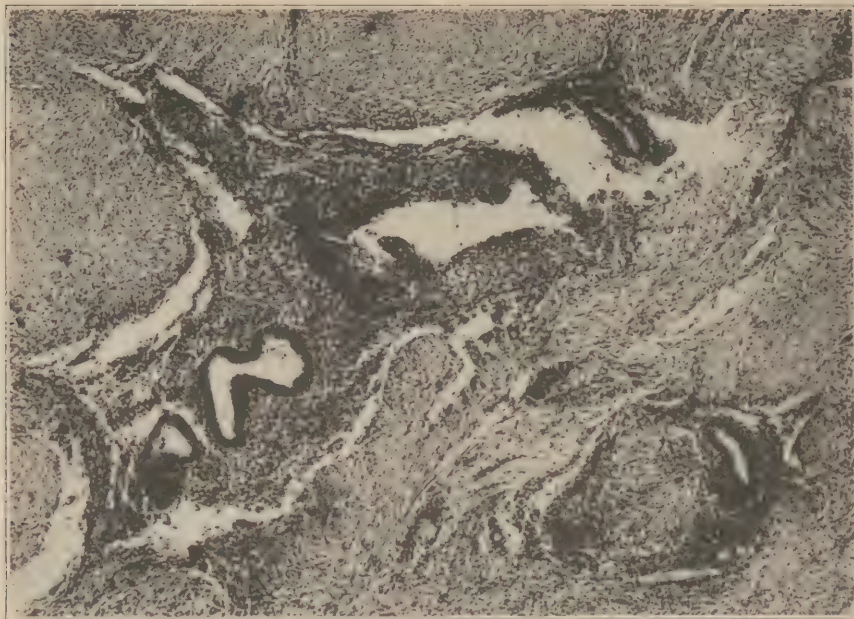
FIG. 86.—Endometrial inclusion in the substance of the ovary. (*C. C. Norris.*)

III. DEPENDING UPON THE PERSISTENCE OF OBSOLETE EMBRYONAL STRUCTURES OR THE DEBRIS RESULTING FROM THEIR IMPERFECT ABSORPTION

PERSISTENCE OF THE INTERNAL AND EXTERNAL BRANCHIAL FURROWS AND OF THE PRE-CERVICAL SINUS

BRANCHIAL FISTULA

Branchial fistulas are rare abnormalities and seem not to have been observed until 1789 when Hensezowski reported two cases. In 1820 Donzi published a paper about them and came to the erroneous conclusion that they opened into the trachea. More correct knowledge began with a paper by Acherson in 1832, in which he showed the mistake of Donzi, and proved that they opened into the pharynx. But it was not until 1890, when the embryological studies of His, Kölliker, Rabl and others had opened the way for correct interpretation, that it can be said the modern consideration of the problem was begun by the important paper by Kostanecki and Mielicki.

According to different authorities the external branchial furrows, the canal of Rabl, the thymic vesicle, the thyro-pharyngeal duct, and the pre-cervical sinus, as well as the internal furrows, tonsillar crypts etc., may be the starting points of fistulas.

But there seems to be little doubt that the great majority of the lateral fistulas arise from the second internal branchial furrow, as regards their deeper part, and from the sinus pre-cervicalis as regards their external part. Okinczyc speaks of them as "satellites" of the pharynx in their deeper part, of the vasculo-nervous bundle in their central part and of the sterno-mastoid in their superficial part.

They are rare. They occur in both sexes, but are rather more frequent in males than in females. Inheritance undoubtedly plays a part in their occurrence, and Acherson observed eight fistulas in three generations of the same family. Fischer found hereditary influence in twenty-one out of 100 cases. Curiously they seem to be more frequent in Germany than in any other country.

Ordinarily the fistulas are unilateral, but may be bilateral. In the latter case the external openings may be symmetrical, or may occur at quite different levels and in different positions.

The internal orifices are constant, always in or near the tonsillar crypts, the external openings vary greatly in position.

Coexistence of cervical fistulas and other facial malformation is rare.

Okinczyc connects the fistulas with the branchial cysts and with the cervical branchiomas because of the complex structure of their walls, in the inner segment of which may be found collections of lymphoid cells, salivary acini and thyroid alveoli derived from the endoderm, and in the outer segment, sebaceous glands, sudoriparous glands, hair follicles, and squamous epithelium from the ectoderm. Numerous mesodermal structures, especially cartilage, derived from Meckel's and Reichert's cartilages of the visceral arches, may also be present.

Some authors divide the fistulas into:

1. Fistulas of primary formation, depending upon malformation.
2. Fistulas of secondary formation, resulting from the opening of a congenital cyst of the neck.

A rather more convenient manner of dividing them is:

1. Fistulas having an external opening only.
2. Fistulas having an internal opening only.
3. Fistulas having both external and internal openings.

I. Fistulas Having an External Opening Only

In a few cases the fistulous passages have been found high up and in the neighborhood of the external ear. To them the name *fistula auris congenitalis* has been applied. One complete fistula of this kind in a much deformed stillborn infant has been reported by Virchow. In that case the outer end of the fistulous passage opened below and externally to the rudimentary external ear, whose external auditory meatus terminated blindly, and the inner end, between the posterior nares and the pharynx. Virchow, followed by von Fröltsch, Ischwartze, König, Burnett and Pflüger, believed that fissura auris congenitalis was the result of persistence of the first branchial fissure. His opposed this view, and explained it as resulting from the imperfect closure of the buds from which the external ear is secondarily formed. In this view he was supported by Gradenzio, and later by Urbantschitch, who showed that the original cleft, even if present, has no connection with the formation of the external ear. There is no actual cleft, the space between the visceral arches being closed by the pharyngeal membrane, which in the case of the first cleft becomes the tympanic membrane, covered on the outside with ectoderm, and on the inner side with endoderm.

But opposed to the view of His that the fistulous passages result from incomplete concrescence of the external ear buds, is the observation that they are frequently present as minute passage-ways parallelling the course of the visceral arches in cases in which the external ear is perfectly formed.

Grunert collected 47 cases of so-called fistula auris congenitalis, in only eight of which was there any evidence of congenital alteration of the auditory organs.

FIG. 87.—Stages in the development of the auricle. (Adapted in part after His.) *A*, 11 mm.; *B*, 13.6 mm.; *C*, 15 mm.; *D*, adult. 1, 2, 3, elevations on the mandibular arch; 4, 5, 6, elevations on the hyoid arch; *af*, auricular fold; *ov*, otic vesicle; 1, tragus; 2, 3, helix; 4, 5, antihelix; 6, antitragus. (*Prentiss and Arey.*)

He believes it better to abandon the misleading name fistula auris congenitalis in favor of *fissura auriculae*, thus definitely referring the disturbance to the secondary developmental processes engaged in the formation of the pinna. In a case which he observed, a three year old girl, there were two, dry, fistulous passages, the larger, ¾ cm. in length, terminating blindly in a kind of sac, the smaller, 2-3 mm. in depth, also ending blindly. Microscopic examination of the wall of these passages showed only ectodermal structures—epidermis with a horny layer, hair follicles, a few sebaceous glands, and occasional sweat glands.

But in the immense majority of cases—cervical fistula—the opening is lower down along the anterior border of the sterno-cleido-mastoid muscle, or between that muscle and the middle line, or even in the middle line of the neck. In the latter position, however, they are apt to be confused with the median fistulas of the neck, which have a different origin, as will later be seen.

The greater number open on the anterior edge of the sterno-mastoid, 2 or 3 cm. above the sterno-clavicular articulation. Some open in the supra-hyoid region, others at the superior edge of the thyroid cartilage.

CERVICO-FACIAL AFFECTIONS OF CONGENITAL ORIGIN

Okinczyc.   "Tête, Cou, Rachis" P. 162

A Enclavomas

I. Teratomas (enclavomas of the blastodermic lines) ....
- Teratomas of the neck.
- Teratomas of the tonsil.
- Teratomas of the thyroid.
- Embryomas of the neck.
- Multilocular cysts of the neck.
- Serous cysts of the neck.
- Embryomas of the tonsil.

II. Embryomas (enclavomas of the blastodermic lines) ....
- Dermoid polyps of the pharynx and of the mouth.
- Branchial epithelioma (malignant) of the neck.

III. Branchiomas (enclavomas of the branchial lines)

1. Solid branchiomas

 (a) Indifferent branchiomas..........
 - Branchioma (benign) of the neck.
 - Mixed tumors of the salivary glands.
 - Mixed tumors of the palatine vault.
 - Mixed tumors of the cheeks and lips.
 - Mixed tumors of the body of the thyroid with slightly differentiated epithelium.

 (b) Endodermal branchiomas
 1. Epithelial salivary branchiomas, derived from the 2nd branchial fissure.
   - Mixed tumors of the salivary glands with differentiated salivary epithelium.
   - Squamous cell carcinoma of the thyroid.
 2. Epithelial thyroid branchiomas (meso-branchiomas) from the thyro-glossal canal and its derivatives.
   - Benign or malignant goiters.
   - Benign or malignant aberrant goiters.
   - Lingual goiters.
 3. Epithelial parathyroid branchiomas, derived from the 3rd and 4th branchial fissures.
   - Benign or malignant parathyroid tumors.
   - Lateral aberrant parathyroid tumors.
   - Inferior aberrant parathyroid tumors.
 4. Epithelial thymus branchiomas, from the 3rd fissures.
   - Thymus gland tumors.
 5. Branchioma derived from the 5th fissure
   - Ultimo-branchial strumas.

2. Cystic branchiomas

 (c) Mesodermal branchiomas..........
 - Branchial fibro-chondromas of the face and neck.
 - Dermoid cysts of the bridge of the nose, outer angle of the orbit, tongue, floor of the mouth, pharynx, palate and neck.

 1. Ectodermal cysts..........
  From the 2nd and 3rd branchial fissures...
  - Lympho-amygdaloid cysts.
  From the 2nd and 3rd branchial fissures...
  - Lympho-salivary cysts (sub-lingual, sub-hyoid, parotid and sub-maxillary.
 2. Endodermal cysts
  From the thyro-glossal canal..........
  - Thyro-nucoid cysts (ranulas with ciliated epithelium, mucous cysts of the floor of the mouth, wall of tongue, neck).
  From the 3rd and 4th branchial fissures..........
  - Parathyroid cysts.

3. Fistulous branchiomas
 1. Primitive fistulas..........
  Internal branchial fissures.
  - Lateral congenital fistulas of the neck.
 2. Secondary fistulas..........
  External branchial fissures.
  - Median congenital fistulas of the neck.

B. Malformations...........
- Atresia, imperforation, adhesions, abscesses.
- Hare-lip.
- True blood cysts—veinoma of the neck.

There is usually a single opening, but there may be several. The external orifice is usually small, and may scarcely admit a fine probe, but it may be so large as to permit the passage of a large sound. It is occasionally guarded by a tag of skin, or cartilage covered with skin, such as form the "auricular appendages" of Sutton, or with skin covered with fine or coarse hairs. Sometimes the opening is at the center of a kind of indefinite cicatrix. It may be at the bottom of an infundibuliform recess, or at the top of a nipple-like structure containing cartilage or bone.

From the opening thin watery, sometimes viscid mucilaginous, or puriform fluid escapes in quantities that vary at different times and may be augmented by swallowing.

Palpation may show a kind of fibrous cord descending into the deeper structures of the neck.

Arrou, Fredet and Demorest describe the course of a probe introduced into the orifice thus: "It usually first descends towards the great cornua of the hyoid bone; the second part of its course bends to reach the digastric muscle, passing between the stylo-hyoid and stylo-glossis, over the posterior belly of the digastric, in relation with the external and internal carotid arteries where they separate, passing between the two vessels. It leaves the facial nerve above, and the glosso-pharyngeal nerve inside of it." Morestin saw one whose abnormal course brought it under the hyoid muscles, under the lateral lobe of the thyroid, against the cricoid cartilage to open in the inferior part of the pharynx.

II. Fistulas Having an Internal Opening Only

Almost without exception the internal opening is to be found in a tonsillar pit, usually in its superior, but sometimes in its inferior portion. In a case observed by Jalaguier, the opening was situated on the posterior pillar of the fauces. Very rarely has it been found in the pharyngo-laryngeal groove, still more rarely at the base of the tongue. Most of these situations can be referred to origin from the second branchial inner furrow.

The size of the opening is variable. It may be very small and easily overlooked, or, as in the case reported by Fischer, so large as to admit the tip of the finger. Large openings may permit food to enter during deglutition, and result in a form of pharyngeal diverticulum.

III. Fistulas with Both External and Internal Openings

It was complete fistulas of this kind that led Cusset and Sutton to suppose that there must have been an actual branchial cleft through whose failure to close the passageway was brought about. How else could there be a passage connecting the pharynx with the exterior of the neck? His is of the opinion that no such passage exists until made by the probe of the surgeon. However, in that he may be wrong, even though his first premise that there was and is no original cleft be correct. Later it will appear that closed tracts sometimes result in the formation of cysts, and that these, later open and become converted into fistulas through pathological change.

Arrou, Fredet and Demorest account for the existence of these fistulas as follows:

Among the ectodermal grooves, the most developed is that included between the second and third arches, the conduit of Rabl. that opens into the pre-cervical sinus. It corresponds perfectly with the depth of the endodermal pocket included between the second and third arches, at the level from which the evagination of the mucosa to form the tonsil appears. At a certain epoch of development, one finds on the inside, the future tonsillar pit, back to back with
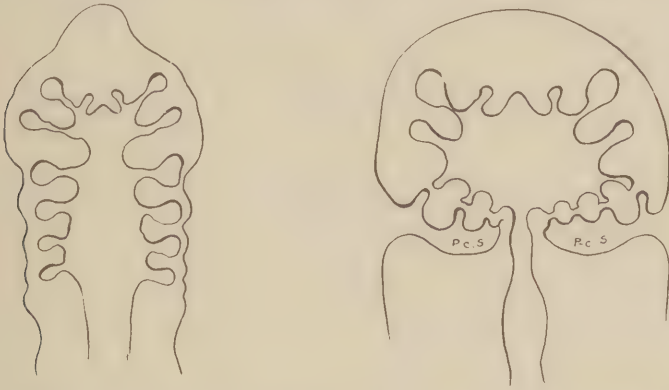
FIG. 88.—Diagrammatic outline of the developing head and neck of a young embryo, showing how the visceral arches, at first in an approximately straight line, as shown on the left, later form a curve, telescoping one over the other, as shown on the right, to form the sinus precervicalis—*p.c.s.* (*Redrawn from Okinczyc.*)

the conduit of Rabl, which through the intermediation of the pre-cervical sinus, opens at the level of the border of the ununited opercular process. If any part of the opercular process should fail to unite with the neighboring parts, the external orifice of the fistula is formed, and thus the varying seat of the external orifice is explained—always below the hyoid bone, and most frequently in the lower part of the cervical region. One easily understands that it may occur in the median line. This explains the fistula that opens externally, but as the conduit of Rabl does not have any communication with the pharynx, and the future seat of the tonsil, it is difficult correctly to account for complete fistulas. In a word, the fistulas that open externally are easily accounted for as arrests of development; the complete fistula cannot exist unless it at some moment abnormally establishes itself by effecting an abnormal communication between the endodermic pouch and the conduit of Rabl. This shows the scheme of Cusset to be absolutely false. The explanation given pemits us to understand the relation of the course of the fistula to the vessels and nerves of the neck. It is acknowledged that the fistulous tract passes between the second and third branchial arches. The facial nerve is in the second arch, hence the fistula ought to pass, as it does, below it; the glosso-pharyngeal nerve is in the third arch, and the fistula passes above it. The third arch being vascularized by the external carotid artery, the fistula necessarily passes above it and comes into contact with the internal carotid artery.

In all cases in which there is an external opening, an internal one ought be looked for. It is difficult, if not impossible, to find it by the use of the probe. as the "knee" in the fistula is difficult to pass, and because of the irregularity of the passageway itself, which is apt to be narrow in some parts, wider in others, cystically expanded in still others. It has been recommended to inject some colored fluid into the external orifice and watch for its appearance at the internal position. In Da Costa's experience this has not met with success. In a few cases milk drunk by the patient, appeared at the external orifice.

FIG. 89.—Microscopic section passing transversely through a branchial fistula at a point at which the passage is divided and lined with columnar ciliated epithelium.

FIG. 90.—Microscopic section passing transversely through a branchial fistula at a point where it is lined with transitional squamous epithelium. The fistulous tract is infected, and both filled with pus and surrounded by inflammatory exudate.

The only surgical treatment for cervical fistulas is complete removal by dissection, a matter that increases in difficulty according to their depth, and is complicated by their close relation to the great vessels of the neck.

Microscopic examination of the wall of a fistula shows an interesting and varied structure. Parts are lined with squamous transitional epithelium, parts with columnar ciliated epithelium, and both kinds may occur in the same field of the microscope, showing that they are not regular in distribution. There is usually a great deal of lymphoid tissue, some of which may be collected into fairly well-formed nodes. Various mesoblastic tissues may also appear.

BRANCHIAL CYSTS

The branchial fistulas are usually sinuses, that is, tracts closed at one end. If, as not infrequently happens, they are closed at both ends, any collection of fluid in the vestigial cavities must result in dilatation and the formation of a cyst. It is thus that the cervical or branchial cysts are supposed to be formed.

If the cyst arise from vestigial remains from an external branchial furrow or from the pre-cervical sinus, it will be characterized by more or less squamous epithelium in its wall, and reminds one more or less of the dermoid cysts. But as a rule the branchial cyst lacks the chief characteristics of the dermoids, has no plastic contents of sebaceous matter mixed with hairs, but is filled with a clear fluid more or less viscid. They are frequently spoken of as *mucoid* to differentiate them from the dermoid.

If it arise from an internal branchial furrow, it may be lined with columnar epithelium that may be ciliated. In some cases linings of both types occur in different parts of the same fistula or cyst.

Branchial cysts are usually first observed about the time of adolescence. They are, of course, congenital, but it seems to require about fifteen years for enough fluid to collect to make them large enough to attract attention. Sometimes it takes longer, and some cases have not been observed before the 30th or 35th year of life.

They are situated in the side of the neck, either behind the sterno-mastoid muscle, or close to its anterior or posterior margin, where they form rounded, ovoid, or cylindrical swellings, well circumscribed, and freely moveable in the transverse direction, though rather less so in the reverse directions. When small they are firm and may be mistaken for solid tumors, but as they become larger, they become softer, elastic, and sometimes fluctuating. The size varies up to that of an orange. It is impossible to discover them when very small, as the sterno-mastoid muscle keeps them from the palpating fingers. They rarely become very large, probably because they have a tendency to open and form an external fistula after the size of a walnut has been reached. Upon first appearance they are commonly mistaken for enlarged lymph-nodes. They are painless, and insensitive, though in rare cases they have been accompanied by neuralgic pains, and more or less pronounced dysphagia supposed to depend upon pressure upon the pneumogastric nerve or upon the pharynx.

They enlarge very slowly. Occasionally they somehow become infected and suppurate. Such cases, whether evacuating spontaneously, or opened by the surgeon's knife, rarely close, but result in a permanent fistula.

There seem to be no recorded cases in which the cystic dilatation has occurred in the inner limb of the tract, and appeared in the pharynx.

They may be above or below the hyoid bone, but unlike dermoid cysts are never attached to it.

FIG. 91.—Branchial cyst.   (*Gould*.)

The only satisfactory surgical treatment is complete removal by dissection, and in performing the operation, great care ought to be exercised not to rupture the cyst, as the dissection then becomes much more difficult.

Microscopic examination of the removed cyst shows its wall to have a structure exactly comparable to that of the fistulous tracts already described. There is a lining that is usually imperfect, and discontinuous, partly composed of squamous, and partly of columnar epithelium, the latter usually ciliated. Beneath the lining, there is usually considerable lymphoid tissue, and on this account, some describe the cysts as amygdaloid or lympho-amygdaloid, under the supposition that they descend from the rudiments of the tonsils.

Anzilatti observed chromaffin cells in the wall of one of these cysts and concluded that they were derived from the rudiment of the para-thyroid body.

Sometimes there are unusual mesodermic derivatives, especially striated muscle, indicating that substance of the arches as well as of the furrows was also included in the structure.

Attention has been called to the occasional occurrence of bits of cartilage at the external orifices of branchial fistula. Such small cartilaginous tags and pendulous formations occasionally occur along the borders of the sterno-mastoid muscle, in the neighborhood of the sterno-clavicular articulation, and in front of the external ear. Sutton speaks of them as cervical auricles, and Lannelongue seems to have been the first to attribute their formation to substance derived from the cartilages of Meckel and Reichert in the visceral arches.

They are really rather appendages than tumors, and are curiosities without clinical significance. They are present at birth, do not grow or change, and are perfectly innocent in disposition. They show cartilage, fibrillar tissue, and occasionally bone, when subjected to microscopic examination.

It has also been pointed out that various tissues, and among them cartilage sometimes appear in the walls of cervical or branchial fistulas and cysts. It is, therefore no matter for surprise that solid tumors should develop from branchial inclusions.

These are very rare, and are much more frequent in the male sex. According to Siegel, the proportions stand 79:6.

The growth of the included embryonal tissue is at first very slow, and passes through a latent or inactive stage that lasts many years. In a few cases the tumors have been noted at the time of birth, but ordinarily they are first in evidence between the 45th and 55th years, in the form of relatively hard rounded movable nodes beneath or at one edge of the sterno-mastoid muscle. They grow slowly, and are, at first painless and without sensation, then commonly take on more and more rapid growth, developing in many cases into malignant and fatal tumors.

Although not infrequently at first mistaken for enlarged lymph-nodes, it soon became evident that they arose where no lymph-nodes were, and that they had peculiar and diversified structure. Some were found to be carcinoma like, others sarcoma like, yet there was no epithelial tissue normally present from which the former could originate, nor yet any lymph-nodes to give origin to the latter.

The first important study of these tumors seems to have been made by Volkmann in 1882. He observed three cases, and came to the conclusion that they arose from branchial inclusions. About a year later, Guttman observed one having much the structure of the thyroid gland, and suspected that it originated from aberrant thyroid tissue. Later investigation of other cases by Veau, Chavassu and Fredet, Beclus and DeFaure, de Reynier, de Moty, and above all by Siegel, have left no doubt as to their branchial origin. So soon as this is admitted, and the tumor brought into line with the fistulas and cysts of the same region, the explanation of all of its peculiarities becomes extremely simple. According to its origin it is an "enclavoma;" according to its position a "branchioma;" and according to its structure a "mixed tumor."

A branchioma nearly always consists of a number of tissues, some adult, some embryonal in type, mixed together in various proportions.

In case the mesoblastic elements preponderate, and the embryonal type persists, the tumor bears a more or less close resemblance to sarcoma; if the ectodermal or endodermal elements preponderates, and the epithelial cells become disorderly and invasive, a more or less close resemblance to carcinoma. If the elements are of adult type, and any embryonal tissue it contains fail to develop excessively, difficulty of classification at once occurs, and in the past was met by assigning the tumor to some group that accorded with the preponderating tissue component, though now-a-days it is sufficient to assign it to the class of mixed tumors.

Every branchioma should be regarded as potentially malignant, and completely and carefully excised as soon as recognized. The latent period is long, but what the particular tumor will do can never be told, and the rule seems to be gradual and persistent advance toward malignant and destructive change. The earlier the tumor is extirpated, the more simple the operation; so soon as infiltration of the surrounding tissue has begun, the difficulty of removal and the probability of recurrence are increased.

The tumor is usually found in the carotid region of the neck, under the sterno-mastoid muscle, close to the hyoid bone. It is at first regularly rounded, and freely moveable, smooth and hard. It grows very slowly at first, but more and more rapidly as time goes on, becoming nodular and shapeless. Before its size seems important, it begins to infiltrate and attach itself to the surrounding structures. In enlarging it may grow upward to the angle of the jaw, or downward toward the clavicle, sometimes displacing the larynx and trachea. It soon infiltrates the tissues below the sterno-cleido-mastoid muscle, and attaches itself to the great vessels of the neck. All three of Volkmann's cases were adherent to the internal jugular vein, and Veau found such adhesions in 28 cases. About the same time or a little later, it adheres to the carotid arteries, after which it moves with them, transmitting the cardiac impulses.

On the other hand, the tumor may attain to a large size before infiltration occurs. In former times when operation was a last resort, the tumors sometimes reached the size of a cocoanut, a child's head, or even an adult's head.

It is an interesting and curious fact that the tumor tends to remain local in nearly all cases. It rarely invades the lymph-nodes, and almost never metastasizes to distant organs. It grows large, ulcerates, gives rise to frequent hemorrhage, through which the strength of the patient is depleted, and by which he is sometimes suddenly destroyed, or it becomes infected, and after a period of local destruction, general infection carries him off. In rare cases thrombosis of the neighboring vessels is the immediate cause of death.

These tumors are apt to become inoperable within a few months from the time they first come under observation. When not removed sufficiently early, they usually recur within a year. The average duration of life after the tumor is known to be malignant, is said to be not longer than two years. A very few cases have no recurrence after operation.

The operation itself is dangerous on account of the relation of the tumor to the great vessels of the neck. Of Siegel's 63 cases, nine died after the operation. Of the 45 cases that recovered from the operation itself, only 20 could be followed,

and of them 15 had recurrences within a year.   Only 5 cases remained free from recurrence for a period of three years after operation.

The tumors frequently give rise to pain of a neuralgic character that may be felt in the tumor or disseminated in the distribution of the superficial cervical plexus, radiating toward the external ear, the temporal and frontal regions, the supra-clavicular and acromial regions, and if the tumor grow into the inferior carotid region, extending down the arm.

Microscopic sections of such tumors may show a simple or a surprisingly diversified structure.

One of the most interesting and unexpected elements is squamous epithelium. In some cases this is so disposed as to give the impression of carcinoma baso-cellulare; in others, like carcinoma spinocellulare, and contains many beautiful epithelial pearls; in still others of no recognized type.   But there may be no squamous epithelium and instead branching and ramifying tubules like ducts— *tubular epithelioma,*—or there may be distinct glandular structures of various kinds—in Volkmann's case like the thyroid gland.

In other cases the epithelial elements are of secondary importance, and embryonal mesoblastic derivatives preponderate, giving the tumor resemblance to the sarcomas.   These cases usually furnish the endothelioma partisans with material for speculation.   But whatever the preponderating tissue, it is usually the ectodermal or endodermal derivatives that occasion the final malignant change.

The definitely "mixed tumor" group, include such of the tumors as contain muscle, cartilage, and bone.   These are usually less malignant than the more frankly epithelial growths.

PERSISTENCE OF THE THYRO-GLOSSAL DUCT

The thyroid gland begins as an exvagination of the primitive pharynx in the neighborhood of the second visceral arch, which descends as the neck develops, until it reaches its normal position below the larynx.   The point of origin is that at which the three portions of the tongue, subsequently to be formed, coalesce, and is known as the *foramen caecum.*   The rudiment is at first a pocket, then as it descends the neck a tube, and finally a solid body of pyriform shape, connected with its point of origin by a filament which ultimately disappears.   Miscarriage of development may determine the persistence of vestiges whose future form will vary according to the time at which the arrest of development took place.   Thus, if it be very early, there may be a tube, open at the foramen caecum, and descending through the base of the tongue to the hyoid bone, or, connecting the hyoid bone with the thyroid body below.   If later, instead of a tube, there may be a fibrous cord, with occasional lumenations, between one or the other of the two structures mentioned, the tongue and the hyoid bone above, the hyoid bone and the thyroid body below.

Such vestiges of the original path of the thyroid rudiment, the *thyro-glossal-duct,* or thyro-lingual duct, as it is sometimes called, are only recognizable in case secondary changes occur as the result of the collection of fluid in the patulous portions, with the subsequent formation of cysts and fistulas.

Occasionally branchial fistulas open in the mid-line of the neck; but they have nothing to do with the thyro-glossal duct, and must be carefully excluded from the present consideration.

It is agreed by Arrou, Fredet and Demorest, and by Sutton, that fistulas resulting from vestiges of the thyro-glossal duct, never appear at birth, but always develop later, as the result of the rupture of a cyst. On this account it seems logical to consider the cysts before taking up the fistulas.

The median cysts of the neck, take origin from persisting vestiges of the thyro-glossal duct, or duct of Bochdalek, and are sometimes called *thyro-glossal cysts*, sometimes *thyro-hyoid cysts* because of their frequent adherence to the hyoid bone. They are not very rare, and are always situated in the mid-line sometimes in the substance of the tongue, sometimes in the floor of the mouth, sometimes below the hyoid bone.

I. Cysts in the Substance of the Tongue

These occupy a median or para-median position in the tongue, and are not in the floor of the mouth, though it may be difficult to determine their exact anatomical relations after they have attained to any considerable size, and it may be necessary to make a microscopical examination by which to settle the matter. They have nothing to do with the thyro-glossal duct, but probably arise, as was taught by von Recklinghausen, who first described them, from the Blandin-Nuhn glands.

II. Cysts of the Floor of the Mouth—Ranula

These have long been collectively known as *ranulas*, and about their origin and nature much controversy has centered, and must continue so long as different cysts having different origins continue to be included in the group.

Lenormant points out that the classical definition of ranula—"an encysted tumor of salivary origin, situated in the thickness of the floor of the mouth"—is doubly incorrect. First, because the Blandin-Nuhn glands, from which the ranulas were first supposed to arise, are not in the floor of the mouth, but in the tongue, and second, because many ranulas are congenital cysts for which no salivary origin has ever been shown.

In looking over the literature the following will be found included among ranulas:

1. Cysts supposed to result from cystic distension and degeneration of the Blandin-Nuhn glands (von Recklinghausen).
2. Cysts supposed to arise from cystic distension and degeneration of the sub-lingual glands (Suzanne, von Hipple, Mintz).
3. Cysts supposed to arise through imperforation of the duct of Wharton. These are very rare, and occur only in the new born.
4. Cysts supposed to be of congenital origin, resulting in consequence of inclusion of embryonal debris at the bottom of the paralingual groove, from which the sub-lingual gland is developed (Imbert and Jeanbrau, Cuneo and Veau).
5. Congenital cysts supposed to arise from vestiges of the thyro-glossal duct (Neumann, Sutton, Okinczyc).

6. Acutely developing cysts supposed to result from inflammation of the sub-lingual bursa— a triangular space situated between genio-hyo-glossus muscle and the mucous membrane, the apex at the frenum, the base at the sub-lingual gland (Fleishman. Tillaux, Boyer).

Any or all of these may exist as definite entities, and may with justification be called ranula. There seems to be good reason for thinking that the more common ranulas are derived from the salivary glands, the more rare ones from the thyro-glossal duct. To differentiate them is however, a difficult matter.

Ranulas ordinarily develop insidiously and painlessly, mostly in the mouths of young women. They form ovoid elevations on one side of the floor of the mouth, sometimes trespassing beyond the median line, and displacing the frenum of the tongue, or, being compressed by the frenum, appearing as a bilobed tumor. They vary in size from a nut to a hen's egg, and are of a bluish or rose color, the surface is free, and the mass fluctuates. There should be little trouble in differentiating them from the occasional dermoids of the same region, because of the plastic contents of the dermoid, and the fluctuating character of the ranula. But in addition, the dermoids have thicker and opaque walls.
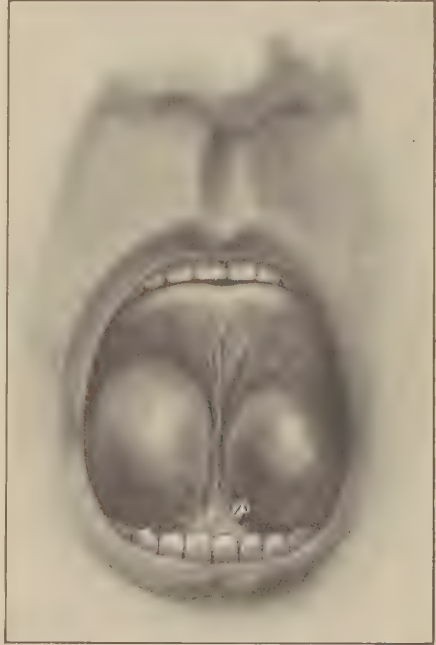
FIG. 92.—Sub-lingual ranula. (*Redrawn from Forgue.*)

They grow slowly, and it is only after having attained to a considerable size that they may embarrass phonation, causing the patient to stutter, or deglutition through the elevation of the tongue. The patient may frequently bite the tongue during mastication. In rare cases they spontaneously rupture, after which they quickly return. They rarely suppurate, and are always benign.

When the cysts are critically examined, they are found to have a thin semi-transparent membranous coverings, of a bluish color, and walls composed of a very thin layer of areolar tissue, sometimes lined with cylindrical epithelium, sometimes only partly so lined, and sometimes without any epithelial lining at all. They are always unilocular, and their contents is always clear, slightly viscid fluid of slightly alkaline reaction. The chemical composition of the fluid differs with the origin of the cyst. Thus, in some cases it is found to contain ptyalin and sulphocyanide of potassium, constituents of the saliva, and suggesting origin from the salivary glands; in other cases both of these constituents are absent, and the fluid is watery, suggesting origin from the vestiges of the thyro-glossal duct.

The upper pole of the cyst is always free, and indeed in many cases the entire cyst is free and can easily be dissected out: such cases may be of salivary origin. In other cases the upper end is free, but the lower either loses itself in the depths of the tissues, or can be traced to the hyoid bone to which it is attached. These cases probably arise from the thyro-glossal duct.

In the cysts supposed to arise from the thyro-glossal duct, the microscopic structure of the wall is of interest. It consists of a fibroconnective tissue containing striated muscular fibres, inside of which is a layer of embryonal tissue composed of rounded cells like lymphocytes, while the whole has, in well characterized cases, a lining of columnar ciliated epithelium. Such structure can only occur in ranulas of thyro-glossal origin.

Lenormant, who seems to believe that ranulas are derived from the salivary glands, describes those that came under his observation as follows:

"When the tumor is really sub-lingual, which is usually the case, it is beneath the buccal mucous membrane, to which it does not adhere, and upon the mylo-hyoid muscle; the gland or its remnants, being pushed downward and outward, so as to adhere strongly to the inferior part of the cyst. The canal of Wharton and the lingual nerve are inside of the tumor, and the canal is always permeable to a probe.

Whatever its position, the structure of the ranula is always the same. It is always a unilocular cyst containing a clear viscid fluid sometimes tinged with blood. This liquid contains in suspension some epithelial cells, and is chemically characterized by increased albumin and mucin. It does not contain either ptyalin or sulphocyanide, and thus differs from saliva.

Upon microscopic examination, the wall appears to be composed of three superimposed layers, which from outside in, are as follows:

1. A fibro-elastic layer containing vessels, and at certain points longitudinal striped muscle fibres. These were first pointed out by von Recklinghausen, and it was upon their presence that he based his conclusion that the seat of ranula was always the Blandin-Nuhn glands, situated in the middle of the muscle fibres of the tongue. Suzanne has also found these fibres, and has shown that they occur in the true sublingual ranulas, as well as in the Blandin-Nuhn ranulas, but in the first case, the striated fibres occur only in the middle line, especially in the posterior wall of the pocket.

2. A layer of embryonal tissue, more or less thick. This was found in all of their specimens by Suzanne, von Hipple, Imbert and Jeanbrau, who recognize it as characteristic. It is marked by numerous vessels with friable walls, which explain the frequent occurrence of hemorrhage into the cysts.

3. An epithelial layer, of which the different authors give different descriptions, probably because the appearances vary in different parts. Robin described a single layer of cylindrical cells; Bazy, ten or fifteen layers of superimposed cells; von Hipple, large cells badly contoured. The type of cell therefore seems to vary according to the cyst examined, and according to Suzanne, the epithelium may be lacking in certain areas. Imbert, Jeanbrau and Mintz, have even examined pockets from which all traces of epithelium have disappeared.

In conclusion, one finds, in the thickness of the cyst wall, especially in the superficial layers, glandular cul-de-sacs which are commonly regarded as lobules of the sub-lingal glands. Cuneo and Veau think them buccal mucous glands. According to the case, these may appear normal, (Robert, Imbert and Jeanbrau), atrophic (von Hipple), Cystic or mucous degenerated (Bazy, Suzanne). Bazy believes that they are ranulas in miniature, from which recurrence may occur after the removal of the primary ranula."

Forgue, who strongly favors the congenital origin of ranula, and looks upon it as derived from the thyro-glossal duct, offers the following as worthy of consideration;

   1. The duct of Wharton is always permeable and can be catherized with a piece of silver wire.   The contents of the cyst is not saliva.

   2. The position of the cyst is opposed to the theory of von Recklinghausen, according to whom it develops from the Blandin-Nuhn glands.

   3. The serous pocket of Fleishmann does not exist; the presence of stratified epithelium on the lining membrane is not compatible with hygroma.

   4. The cystic transformation of the sub-lingual gland, with mucous degeneration, is without known cause, has not been observed by other authors, and could not in any way explain how the cyst could have a lining of ciliated columnar epithelium.

He concludes that it is easy to account for all of the peculiarities of the cysts by assuming that they are congenital, because of their structural identity with the branchial cysts, and agrees with Neumann and Sutton that they are derived from vestiges of the thyro-glossal duct.

The reader must keep in mind that the slowly forming cysts under consideration, have nothing to do with the occasional retention cysts of the sub-lingual and sub-maxillary glands that occur acutely as the result of infection and closure of the ducts.   Behind such obstructions saliva accumulates rapidly, pressing the tongue upward so that it seems to become glued to the palate, making deglutition difficult, and sometimes threatening and even causing asphyxia through edema of the sub-mucous tissue (Lefort and Duplay).   When such an accumulation is relieved by spontaneous rupture or incision, immediate relief is afforded, and recovery takes place rapidly without recurrence of the cystic accumulation.

III. Cysts in the Mid-line of the Neck

These are also called *sub-hyoidian ranulas*.   They occur in the mid-line of the neck, below the hyoid bone, sometimes alone, sometimes in association with sub-lingual ranula, and it occasionally happens that when one is extirpated, the other appears.   According to Lenormant, they are "infinitely more rare than sub-lingual ranulas."

It is interesting to see that Lenormant, who, it will be remembered believes sub-lingual ranulas to be derived from the sub-lingual glands, attributes subhyoidian ranulas to the same origin, and with Cadio and Gosselin regards the latter as but recurrences of the former, which embarrassed in their growth towards the mouth, by the presence of the operation scar, insinuate themselves through the hyoid muscle, and appear under the skin. He, however, admits that this

Fig. 93.—Hernial passage of prolongations of the sub-lingual salivary gland between the fibers of the mylo-hyoid muscle. (*Morestin.*)

conception is not applicable to those cases in which there has been no previous extirpation of a sub-lingual ranula, or to cases in which the cyst in the

floor of the mouth co-exists with one in the neck. But as Morestin has seen
cases in which the sub-lingual glands made hernial passage through the maxillary
insertion of the mylo-hyoid muscle, by separating the muscle bundles, he believes
it easy to understand that these prolongations may degenerate at the same time
as the principle part of the gland, or may do so independently of it, in which
latter case there would be only the ranula in the middle of the neck.
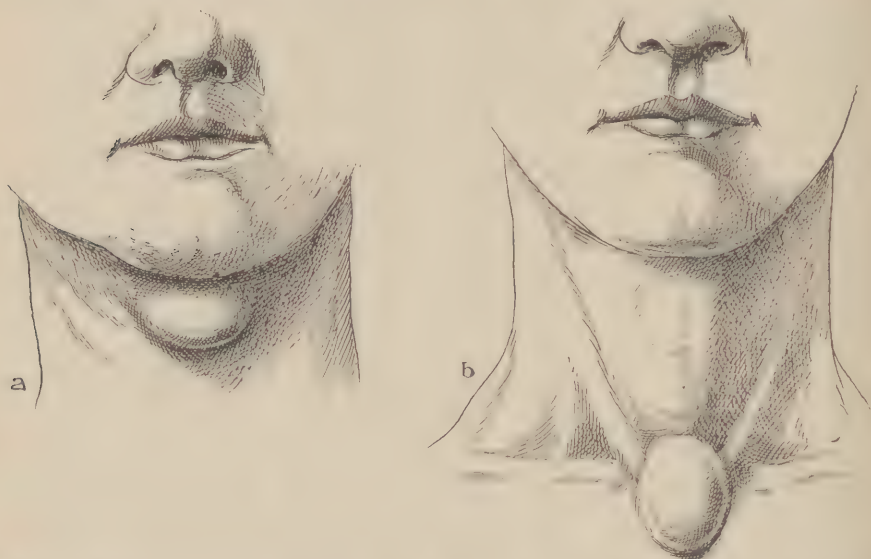
FIG. 94.—Median cysts (thyro-glossal cysts) of the neck.   *a*, In the neighborhood of the hyoid
bone; *b*, in the supra-sternal notch.   (*Redrawn from Le Dentu and Delbet.*)

But is it not much more easy to accept the view of so many of the other
writers quoted, and suppose that these cysts arise from the persistence of an
embryonal structure situated exactly where the cysts occur, which brings the
formation into line with other well recognized congenital defects? If this does
not seem so at present, it may become so when the median cervical fistulas are
considered. But before leaving the subject, it will be well to note that in a
contribution as late as 1921 J. E. Thompson speaks of ranula in these words:

I have adopted the theory that ranula, sub-maxillary cyst, and deep cervical cyst—are
derived from the cervical sinus which has been carried from its original position by the muscles
of the branchial arches and those of the hypoglossal segments during the process of their migra-
tion. On this theory, the deep cervical cyst, which has such characteristic anatomical bound-
aries would be carried upward by the palate muscles, all of which except the tensor palati (first
arch), are derived from the third and fourth arches, whereas the cysts found in the sub-max-
llary and sub-lingual regions would be carried upward by the muscles of the tongue derived
from the hypoglossal group, which belongs to the seventh, eighth and ninth body segments."

That the branchial fistulas may occasionally open in the midline of the neck,
has already been mentioned, and was pointed out by Arrou, Fredet and Demo-
rest. If the fistulas can do so, the cysts may also occasionally develop there.
But the occurrence is most exceptional. It seems more simple to suppose that

the cysts arise from structures normally situated where they occur, than that they arise from some other structures away from that situation, and are subsequently transplanted to it.

Among 86,000 consecutive patients examined in the Mayo Clinic, only 31 thyro-glossal cysts were found. Sistrunk, who analyzed them, states that 18 occurred in males and 13 in females. They appeared at all ages from birth to 53 years, the majority being noted in patients from 20 to 25 years of age. In 25 of these patients the cyst was found in the mid-line of the neck, near the hyoid bone.

In regard to the structure, both gross and microscopic, the cysts of the middle of the neck, do not differ from those of the floor of the mouth. The same embryonal tissue, and the presence of ciliated columnar epithelium are to be accounted for.

Median Cervical Fistula

As has been pointed out, a few of these may be branchial fistulas, that by accident have their openings in the middle line. But most of them are different not only in position, but also in their clinical manifestations. Thus, according to J. B. Sutton, they are never congenital in the sense of being present at the time of birth, but make their appearance much later, usually about adolescence, that is about the 14th year. They always open in the middle line of the neck, between the hyoid bone and the supra-sternal notch, the most frequent seat being at the level of the cricoid cartilage. They may appear spontaneously, as the result of the rupture and evacuation of a swelling, or as the result of the prick of the surgeon's lancet. Arrou, Fredet and Demorest believe them aways to be secondary to the rupture of a cyst, but assert that this only applies to those situated above the thyroid cartilage, as those below it do not differ from the lateral fistulae, and open internally in the tonsillar pits. Their experience, however, differs from that of others, notably Sutton, who states that if a probe be introduced into one of the sub-hyoidian fistulas, it passes upward to the hyoid bone in the mid-line of the neck, directly beneath the skin, and stops at the lower border of the hyoid bone. He also states that in some cases vestiges of the thyro-glossal duct were visible as a conspicuous ridge ascending the mid-line of the neck above the fistulous opening which is usually situated in a scar-like formation on the skin.

In a case observed by the author, the fistula occurred in a young girl of about 15 years of age. Near the hyoid bone there was a small lesion like an encrusted papule. For weeks at a time this would be dry and somewhat scaly, and an indefinite swelling occurred in the neighborhood. A slight discomfort directed the patient's fingers to the disturbed region and sooner or later the scab would be detached, when there would be an escape of clear watery fluid, drop by drop, for a few days, causing much annoyance. About the time her patience became exhausted, the scab would form anew, and there would be another dry period. This continued for many years, until the patient was lost sight of.

In that case there was nothing unsightly, but in some cases the opening of the fistula is larger, and being situated lower down in the neck, is conspicuous, and the oozing fluid annoying because it moistens the clothing. The fluid is sometimes thick and mucilaginous.

Microscopic examination shows these fistulous tracts to have a structure sufficiently different from the lateral fistulas to make their separate origin

FIG. 95.—Median cervical fistula of thyro-glossal origin. (*From "Tumors, Innocent and Malignant," by Sir John Bland-Sutton.*)

almost certain. They consist of a tube lined with ciliated columnar epithelium, in the walls of which there is apt to be an occasional deposit of thyroid tissue. The presence of the latter, and the absence of the miscellaneous mesoblastic derivatives found in the lateral fistulas, seem good ground for believing that the median fistulas arise from vestiges of the thyro-glossal duct, while the lateral fistulas arise from the pre-cervical sinus and branchial furrows.

Finally, the only solid tumors that occur in the path of the thyro-glossal duct, and from its vestiges, seem to be the aberrant thyroids already described; no branchiomas ever arise in the middle line, or from the vestiges of the thyroglossal duct.

PERSISTENCE OF THE DENTAL SHELF

Certain tumors of the jaws cannot be understood without an acquaintance with the general principles of the development of the teeth.

According to Heisler, the teeth, morphologically considered, are calcified papillae of the skin, capped by a layer of peculiarly modified and calcified cells of the epidermis. The dentine and cementum, as well as the pulp, are mesodermal derivatives; the enamel is ectodermal.

The first indication of the position of the future teeth, makes its appearance during the sixth week of embryonal life in the form of the "dental ridge" or "dental shelf," which is a continuous layer of ectoderm that enters the jaw at right angles to that which working its way upward

Nasal pit

Eye

Median position of the palate

Dental ridge

Lateral portion of hard palate
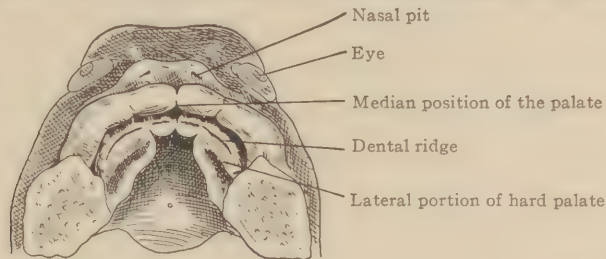
FIG. 96.—Diagram showing the development of the roof of the mouth and dental ridge. (*His.*)

or downward in a vertical direction, eventually separates the lip from the gum. Entering the outer side of the jaw, it takes an oblique upward and inward direction toward the lingual surface.

At first consisting of a more or less uniform layer, the dental ridge, during the third month of embryonal life, begins to change through the downward growth of ten flask-shaped processes, whose positions correspond with those of the ten teeth of the first dentition. They soon become separated from one another, and from the exterior, through atrophy of the remaining ectodermal substance, and later invaginated below by an upward growth of a portion of the mesoderm into each. These are the dental papillae, by which the dentine and cementum will be formed, and the epithelial caps which cover them will form no other part of the teeth than the enamel by which the crowns are covered.

Before the actual formation of the milk teeth begins, each ectodermal bud gives off another secondary bud, to provide for the second or permanent teeth to follow them, and from the lateral edges of the dental shelf, extension of the ectoderm towards the temporo-maxillary articulation, years later, provides for three additional thickenings on each side, and in each jaw, to prepare the way for the twelve additional teeth of the permanent dentition.

The enamel and dentine of the temporary teeth are begun during the 17th

FIG. 97.—Transverse sections through the lower jaw showing the formation of the dental shelf in embryos of (*A*) 17 mm. and (*B*) 40 mm. (*Röse.*)

week of embryonal life, and the rudiments of the permanent teeth are begun at the same time. The actual development of the permanent teeth comes much later, and the rudiment of the third molar is not seen until about the fifth year after birth.

As has been said, the ectodermal caps superimposed over the dental papillae, have a single function, that of providing the enamel, and with that object in view, develop at once into what may be described as the enamel organ, or as it is frequently called, the adamantine organ. Originally the general appearance of the cells much resembles the squamous epithelium, but as differentiation progresses, the cells nearest to the dental papilla, begin to acquire an elongate form, and to resemble columnar epithelium arranged in a definite layer. These are the *ameloblasts*. Soon the columnar form is definite, and the cells beyond that row disappear,

FIG. 98.—Developing tooth germ. ×300. *a*, Tooth band; *b*, oral epithelium; *c*, layer of infant cells; *d*, stellate reticulum; *f*, dentine papilla. (*Broomell and Fischelis.*)

after a period of what is sometimes called enamel pulp. The enamel itself is the result of the direct transformation of these cells, which calcify, beginning at the basal portions, and continuing throughout. Each cell is thus transformed into what is called an enamel prism, with the exception of its outermost portion where a thin layer of protoplasm remains, and forms the enamel membrane which is worn off soon after the eruption of the teeth.

The mesenchymal cells of the dental papilla soon become differentiated into connective tissue, into which vessels and nerves penetrate. Its superficial cells develop as odontoblasts which form dentine much the same as osteoblasts manufacture bone; the only important structural difference between dentine and bone being that in the former the protoplasm of the odontoblasts is drawn out into long slender, parallel processes, that fill the dentinal canals, while in the latter branches of the osteoblasts ramify and accommodate themselves to the lacunae and canaliculi. The dentine of the root of each tooth eventually acquires a layer of true bone, the cementum, by which it is united firmly to the walls of its socket.

Certain facts concerning the enamel organ are of great importance. First of all must be considered the process of budding by which the rudiments of successive teeth are provided for. In man this is so limited that only a first and second dentition result. Having but two sets of

teeth, man is described as a *diphyodont* animal. There seem to be no theoretical grounds upon which it can be said to be impossible for him to have three sets of teeth, but no thoroughly trustworthy cases have yet been reported. However, many of the lower animals are continually having new buds extend from the enamel organ and are continually producing new teeth to take the places of those lost or worn out. Such animals are known as *polyphyodont*, and the sharks will serve as examples.

Second, is the original continuity of the dental ridge, with the disappearance by atrophy of the connections between the developing enamel organs and the outer ectodermal tissues.

If an enamel organ instead of producing one bud should, as the result of some unknown stimulus keep on budding, and the buds give off auxiliary buds, it will be seen that eventually a very complicated enamel producing structure, devoid of tooth relationship might be produced. In fact such things are occasionally met with, and receive the name *adamantinoma*.

If the connections between the developing adamantine organs and between them and the external surface of the jaw did not undergo the customary atrophy, there would remain debris whose subsequent growth might result in tumors.

Adamantinoma

It has already been observed that the ectodermal cells clustered to form the caps over the dental papillae, and destined to form the enamel, have close resemblance to squamous epithelium, but that as they embrace the papilla more and more closely, and their cells prepare for their final purpose, the innermost become distinctly cylindrical, and the others disappear by atrophy. Should perversion arise, and tumor growth arise from these cells, it is easy to understand that according to the development to which the cells had attained, the histological details of the tumor would vary, and that if different parts of it underwent different degrees of development, those parts might have different appearances. Thus, in all probability, there come about, in the jaw, a number of tumors in which may be found collected and ramifying squamous epithelium, looking like squamous epithelioma, and sometimes containing epithelial pearls, and other collections of undifferentiated epithelium, the outer layer of which is distinctly columnar, and the centers of which may be melting away into cystic spaces, and spaces surrounded by columnar epithelium in single row, as in glands, and the denser parts of which may contain scattered enamel prisms or masses. The continued budding of the enamel forming tissue, the various stages of development it represents, and the invasion of the epithelial structures into the bony and fibrillar substance of the jaw, may thus eventuate in enormous solid and cystic tumors, that, on account of the generally invasive tendency of the epithelial elements incline to be and sometimes are malignant. Bryck observed one such tumor that weighed 1.5 kg. Ewing observed at autopsy "a solid tumor of the upper jaw as large as a child's head, projecting internally into the naso-pharynx with dysphagia, and externally into the orbit with exophthalmos."

Adamantinomas are not necessarily limited to the jaws; they may occur elsewhere, as in dermoid cysts and teratoma, if tooth germs are present. B. Fischer has described what he regarded as an adamantinoma of the tibia, supposed to have arisen through modification of the surface epiderm, but it is difficult to believe that this was not some other kind of tumor with resemblances suggesting adamantinoma.

When examined microscopically, adamantinomas are found to be chiefly composed of a branched epithelial reticulum, composed of fine and coarse branchings, not unlike certain forms of carcinoma. Transverse and oblique sections through these processes reveal only indifferent cells, and do not assist in making the diagnosis, but when they pass through the larger cell masses they reveal an interesting and significant diversity of structure, for the outer layer of cells is of cuboidal or columnar shape, closely resembling the ameloblasts, the next few rows of cells indifferent in form, while the inner cells fade imperceptibly

Fig. 99.—Adamantine epithelioma of the upper jaw of 10 years duration in a colored woman 50 years of age. (*Halsted and Bloodgood.*)

into a delicate and loose reticulum of multipolar cells whose processes connect, leaving a meshwork of fine fibrillae such as is seen in mucoid tissue—the "star-like reticulum." In the largest cell groups the centers sometimes appear as empty spaces. These may undergo cystic distension by which the surrounding epithelial cells are compressed against the connective tissue, so as to flatten and lose the resemblance to the enamel organ altogether. In such cases, in which no star-like reticulum can be found, it may not be possible to recognize the nature or histogenesis of the tumor, which may then be called adeno-carcinoma.

There is a not inconsiderable resemblance to carcinoma basocellulare, especially that variety of it known as benign cystic epithelioma, and it is not impossible that the latter lesion has occasionally been mistaken for adamantinoma by those not entirely familiar with it, or concious of the importance that is to be attributed to the presence or absence of the starlike reticulum.

Adamantinomas usually make their appearance in adult life, but Choate has reported one that occurred in a child of six years, and Börnig one in a man

of seventy. Women seen to be afflicted most frequently. The tumors occur
in either jaw, and it is said that the upper yields the greatest number of solid,
the lower the greatest number of cystic growths.

They always grow very slowly, and may not be very large after 25 years.
Albarran observed one that had been growing for 38 years. Small tumors
of this kind may be easy or difficult to remove according to their circumscription,
large ones are usually inoperable but in all cases the prognosis is bad because of
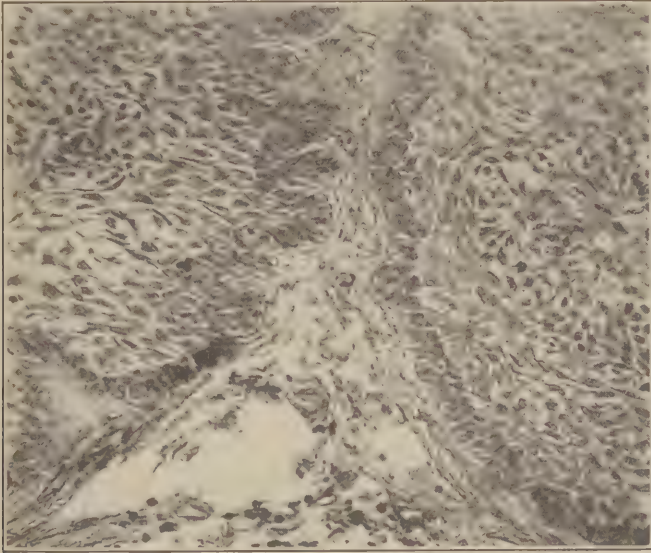
Fig. 100.—Microscopic section of an adamantinoma, showing the row of ameloblasts at the
periphery, and some of the cells of the starlike reticulum at the extreme left. (*Photomicro-
graph by Prof. Allen J. Smith.*)

almost certain recurrence from buds left behind. Repeated excision, followed
by repeated recurrence is said to result in a change in the general type of the
structure, which grows more rapidly, is more cellular, and becomes more
malignant.

The malignant adamantinomas are invasive and destructive, but rarely
metastatic. Ewing saw one, which he described as a "fibro-epithelial" tumor,
that was accompanied by metastasis to one cervical lymph node, and had one
node in the lung.

Odontomas

Odontomas are tumors occurring in connection with the teeth. It seems
probable that they arise from the vestiges of the connections between the
developing enamel organs, and them and the surface covering—what Albarran
has called the *para-dental debris*. This, he describes as a kind of mesh-work
that surrounds a tooth much as its net surrounds a balloon, and which can be
divided into three different portions:

1. A superficial or gingival portion, situated below the mucous membrane of the jaw or gum.
2. A median portion on the thickness of the gum, between the mucosa and the tooth follicles.
3. A deep portion, buried in the jaw in relation with the roots of the teeth.

The cells that enter into the composition of this debris are in general of polyhedral shape and of small size; in a few of the larger cell masses, however, there may be cylindrical cells.

FIG. 101.—A dentigerous cyst in which a bicuspid tooth forms the nucleus. In this case there were three bicuspid teeth on the right side of the mandible. The patient was 14 years old. (*Brophy*.)

Tumors, cystic tumors, and cysts may arise in connection with the teeth in several ways. Thus, the formative energy may be misapplied in such manner that instead of a normal tooth, a large mass without shape, and composed of a miscellaneous commingling of the tooth elements in various stages of differentiation, results. Or, the epithelial elements set aside for the production of the enamel, failing to connect with the normal papillae, develop independently of

them, and produce a confused mass of epithelial gland-like tissue, that is scarcely to be recognized as transformed enamel organ (adamantinoma). Or, the para-dental debris may take on unexpected development, and give rise to a considerable mass of tissue of so varied appearance as to be very puzzling to whomever undertakes to discover its histogenesis.

If the tumor mass result from the perverted development of a tooth, it must naturally take the place of that tooth, which will, in consequence, be lacking. But if it arise from the para-dental debris, it may be in intimate relation with the

Fig. 102.—Roentgenogram of a dentigerous cyst in situ. (*Brophy*.)

tooth, or have no relation with it, according to the position of the para-dental debris concerned, which may lie between the teeth, at the roots of the teeth, or in the gums about the teeth.

If the tumor arise from the tooth germs themselves, the commencement of its growth must coincide with some stage in the development of the tooth, which usually means very early in life. If it arise from the para-dental debris, it may begin at any period of life.

But although arising from the para-dental debris the condition of the contiguous tooth or teeth may suggest the time at which development began. Thus, if very early, the tooth might show deformity; if late, it would escape. If from para-dental debris remote from the tooth, there would be no effect at all.

Broca endeavored to classify the tumors of dental origin according to the time at which their development began:

1. *Embryoplastic Period, and Embryoplastic Odontoma.*
   This period precedes the appearance of the dental tissues, and the tumors arising during it, reproduce the structure of the dental bud, either remaining in the embryonal stage and forming a soft tumor composed of embryonal cells distributed throughout a mucous matrix, or advancing beyond this stage, assuming the characters of a fibroma.
2. *Odontoplastic Period and Odontoplastic Odontoma.*
   This is characterized by the appearance of the essential and peculiar tissues of the tooth—dentine and enamel. The tumors of this period are characterized by the presence of these tissues.
3. *Coronary Period, and Coronary Odontoma.*
   This is the period during which the crown of the tooth is completed, and the enamel surmounting the dentine or ivory formation perfected. The odontomas of this period comprise circumscribed growths about the necks of the teeth.
4. *Radicular Period, and Radicular Odontomas.*
   It is during this period that the dentine of the root of the tooth is formed, and the tooth erupts. The radicular odontomas occur solely about the roots of the large molars, and are the only tumors of the class that contain cementum and are firmly attached to the roots. They are first found when the tooth is extracted, being drawn out with it, even when the size is large.

As the development of any of these tumors, in any of the stages mentioned interrupts or modifies the evolution of the tooth with which it is in relation, and is accompanied by the formation of a new growth, it is invariably characterized by the appearance of swelling of the jaw, usually in the neighborhood of the large molars, and commonly at a position where a tooth is absent. The single exception is the radicular odontoma, whose existence may not be suspected until the tooth to which it is attached is extracted, when the tumor is brought to light.

Dentigerous Cysts

The cysts of the jaw appear somewhat different clinically and morbid-anatomically, but have much the same etiology as its tumors, and the one should never be considered without the other.

I. *Small Radicular Cysts.*—These were first described by Delpech, and are small cysts rarely larger than a hazel nut, attached to the roots of the teeth with which they are not infrequently removed during extraction. Forget called them *alveolo-dental cysts;* Magitot, *periosteal cysts;* Aguillon, *radicular cysts;* Malassez, *radiculo-dental cysts.* It was the last named author who first attributed their occurrence to the deeper para-dental debris.
   The wall of the cyst is in intimate relation with the tooth, but the tooth is separated from the cyst contents with which it never comes into contact. In some cases the two are separated by a longer or shorter pedicle. The cyst wall is usually fairly thick; the contents are usually clear and viscid, but may be cloudy and buttery from the presence of fat and epithelial cells. The epithelial lining consists of cells of varying type, and from it prolongations commonly penetrate into the tissues of the cyst wall. Squamous epithelium of transitional type is common, but in nearly all cases, the type of cell changes as the surface is reached, and the cells become columnar as in the enamel organ. When these are not present, the uppermost cells are usually flattened by pressure contact with the contents of the cyst.

If suppuration of the cyst wall follows infection, the epithelium may be destroyed or unrecognizable, and the cavity resembles an abscess, and it is not impossible that some abscesses of the jaw have this origin though it is not suspected.

These cysts are usually solitary, but may be multiple, and Wilks saw a child 12 years of age in whose mouth five were found attached to the roots of as many teeth. Witzel found them more frequent in the lower jaw, the proportion being 76:29.

FIG. 103.—Dentigerous cyst of upper jaw, of 13 years duration in a colored girl 19 years of age. There was parchment crepitation; the teeth were normal. (*Bloodgood*.)

Their origin seems best explained by assuming with Malassez that they arise from the deeper para-dental debris during the fourth period of Broca, i.e.. after the general formation of the tooth has been completed.

II. *Dentigerous Cysts.*—These are also called *Corono-dental Cysts*, and undoubtedly arise through malformation of a tooth, and always occupy the position of a tooth that is missing, deformed, or included in the cyst itself. In the latter case, the tooth usually lies in a horizontal position which makes its eruption impossible. The tooth may be free in the interior of the cyst, or partly embedded in its wall. In either case it is apt to be badly deformed, especially about the root, which is the last part to be perfected. Such cysts are always unilocular, though occasionally one contains two teeth. This appears as though there might have originally been two cysts which united, but there are cases in which more teeth are found, and Grosse has seen one cyst in which there were eight. These are difficult to explain, and lead to the consideration of a somewhat different kind of cyst, the *Multilocular Dentigerous Cyst* or *Compound Follicular Odontoma.*

In these, instead of a simple cyst, there is either a single cyst with auxiliary pockets in its walls, or a congeries of separate or communicating cysts, in which, without any regularity of distribution, many, mostly rudimentary, and usually badly formed teeth occur. In a case reported by Windle and Humphries 40 such denticles were found in a cystic tumor taken from the mouth of a little boy of ten years.

Nearly all of the patients in whom such tumors occur, are young; usually between 10 and 20 years. When they occur later, say between 20 and 30 years, they are nearly always connected with the wisdom teeth. This seems to be additional confirmation of the fact that they form during the development of the teeth.

From such compound follicular cystic odontomas, in which a considerable and indifferent matrix holds together a considerable number of cysts, each containing a number

FIG. 104.—Boy of 9 years of age with a dentigerous cyst of the mandible involving the central and lateral incisors, cuspid and both bicuspid teeth. The cyst was accompanied by an extensive fibrous growth. The teeth were completely concealed from view by the growth. The upper teeth made deep impression in the growth. The cyst and tumor were removed intra-orally. Three months have elapsed without recurrence. (*Brophy.*)

of more or less imperfect teeth, it is but a step to another group of tumors, called by Sutton and others, *Composit Odontomas*, which are characterized by a kind of reversed structure. That is, large or relatively large masses of dense tooth structure, irregularly compacted, and without intervening partitions, or cyst formation. Such masses, composed of enamel, dentine, and cementum, bear no other resemblance to teeth than that they are composed of the histological elements of tooth structure. Occasional cases occur that are, in a certain way intermediate between the two forms just described, as in one reported by Hildebrandt—a little boy of nine years, with normally erupted but malplaced teeth, whose jaws were distended by a mass composed of some 200 supernumerary, separate or variously fused teeth, most of which were fairly well formed. At subsequent operations as many more were removed, and the jaw bone, reduced to a thin shell was curetted, with the result that in the matter scraped out, many more rudimentary teeth, enamel organs, and para-dental debris were found.

FIG. 105.— Portion of a dentigerous cyst with a tooth attached. (*Bowlby and Andrewes.*)

EPULI

An epulis is a tumor that grows upon the gum. It usually takes the form of a node, but may be polypoid or fungoid, and may be single or multiple, always

arising about the necks of the teeth. It rarely attains a size greater than a hazel nut before the patient seeks advice, and commonly has it removed.

When subjected to microscopic examination, these tumors are found to present a variety of appearances, and are divisible into the simple or benign and the complex or malignant. But the subsequent history of the case does not always correspond with the expectations based upon the microscopic diagnosis and prognosis. Many are composed of fibrillar and vascular tissues, and are undoubtedly benign; some are more highly cellular, and resemble spindle cell sarcoma, some are characterized by large numbers of giant cells, and like giant cell sarcomas; a few are distinctly epithelial and resemble squamous cell carcinomas.

Many believe that these tumors arise from the tissues of the mucous membrane, the periosteum, or the bony tissue of the jaw, but Malassez is of the opinion that they arise from the para-dental debris of the gingival margins. This origin would be consistent with the variety of histological appearances presented.

In general epuli are benign in disposition. If thoroughly eradicated, they usually do not return, but in some cases they do and the jaw may be invaded. Those showing structure resembling myxo-sarcoma are prone to recurrence, those of carcinomatous structure behave as such.

PERSISTENCE OF THE EMBRYONAL TAIL

That the embryonal tail, instead of disappearing, occasionally develops along lines more or less corresponding with what takes place in lower animals, has already been pointed out, and the appendages described.

The sacral, like the maxillary region, is an occasional seat of embryonal parasites, known as *epignathi* when attached to the superior maxillary bone, *sacral parasites* when to the sacrum. They are usually recognizable by inspection, or dissection, but if without definite members or organs, and composed of confused tissue masses it may not be possible to distinguish them from tumor-like masses that arise from the vestigial structures of the embryonal tail, and are collectively known as *sacro-coccygeal tumors*.

When one considers the number of temporary structures the embryonal tail contains, the vestigial survival of any one of which might result in tumor growth, it is less surprising that such tumors arise, than that they do so infrequently.

But lest the latitude given by the possibilities mentioned should make it appear that any or all morbid growths of the region fall into the group of sacro-coccygeal tumors, the following well characterized conditions must be excluded: Spina bifida and spina bifida occulta with superimposed fatty tumor; dermoid cysts; pre-sacral and pre-coccygeal mucoid cysts of the post anal gut, and the amorphus tail-like appendages.

When this is done, there still remain a few highly complex tumors, the true sacro-coccygeal tumors.

They are usually present at the time of birth, most frequently in female infants, and are sometimes so large as to cause dystochia. In some cases the tumor at the time of birth is small; more often it is large. Sometimes its bulk is

10

more than half that of all of the body of the child. It may be sessile when small, but becomes pedunculated and pendulous when large, and hangs from the coccyx, as may be felt by combined external and rectal examination, supplemented by X-ray examination. It is covered by skin which is smooth and natural in appearance. The substance may be firm, or soft, or varying, and fluctuating in parts where cysts are probably present. The general appear-
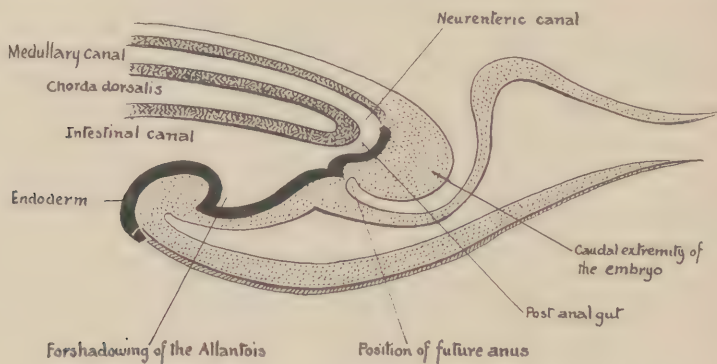
FIG. 106.—Longitudinal median section of the posterior extremity of a human embryo, showing the structures that enter into the composition of the human tail. (*Redrawn from Okinczyc.*)

ance is like a large cushion hanging between the legs of the child, upon which it seems to sit.

In very rare cases similar tumors develop later in life from beginnings inconspicuous at the time of birth. One case is on record in which there was scarcely any growth until the 32nd year, when the tumor began to grow rapidly.

When one of these tumors is dissected, the skin and superficial fascia readily separate, leaving the tumor proper enclosed in a fibro-connective tissue capsule.

But as the matter of dissection is pursued difficulties arise. Either the tumor proves to be an amorphus mass of different tissues, or definite structures recognizable as organs are found. As has already been said, if these can be brought into such order as to show the structure to be a parasitic embryo, it ceases to be sacro-coccygeal tumor.

The discovery of derivatives of the three blastodermic layers in a circumscribed morbid growth is usually sufficient to show it to have developed from a second germinal cell or from a separated blastomere.

But it is not necessary to fall back upon either a germinal cell or a blastomere to account for the tri-blastic structure of a sacro-coccygeal tumor; it arises where vestiges of rudimentary structures from all three blastodermic layers are normally already present. In the embryonic tail are to be found ectodermal derivatives from the external covering and from the medullary canal, endodermal derivatives from the post-anal gut, and mesodermal derivatives, in the form of the superfluous coccygeal vertebrae, and a certain quantity of substance derived from the sclerotomes and myotomes. The tumors share many of the characteristics of the mixed tumors.

FIG. 107.—Sacro-coccygeal tumors. That on the left, in the pathological museum of the University of Pennsylvania, is a teratoma; that on the right, redrawn from Kirmisson, was regarded as a mixed tumor.
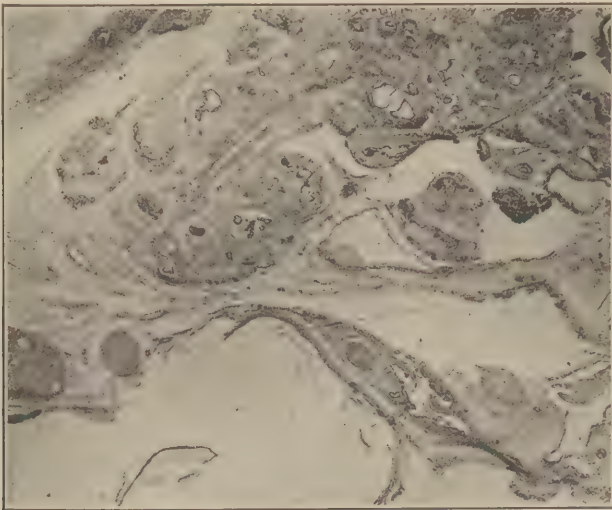
FIG. 108.—Microscopic section of the sacro-coccygeal teratoma shown in the preceding illustration. The greater part of the field is taken up by a glandular tissue more closely resembling the mamma than any other organ. It was partly upon its presence that the diagnosis of teratoma was made. (*Photomicrograph by Prof. Allen J. Smith.*)

The connective tissues form the preponderating structural elements, and usually show more or less confused intermingling of fibrillar, cartilaginous, mucoid, osseous, and muscular elements. Cysts may occur, sometimes as the result of necrotic softening, sometimes as definite formations lined with stratified squamous epithelial or with columnar epithelial cells. Both varieties of epithelium may be found in the same cyst. Sometimes the columnar epithelium is ciliated.

Most of the cysts are mucoid, some are undoubtedly dermoid.

The tumors may spring from the anterior, the posterior, or both surfaces of the coccyx. If anteriorly only, they grow into and fill up the pelvis, obstructing the fecal and urinary passages, and causing the early death of the child. If posteriorly only, and relatively small they may be mistaken for the amorphus tail-like appendages.

When it arises from both surfaces, it hangs between the legs and becomes pedunculated.

In some cases the tumors grow rapidly; in others little progress is made during many years, but if, an indolent tumor begins to grow later in life, it usually makes up for lost time.

Ordinarily, however, the tumor shows no signs of malignancy. It does not cause metastasis, either to the lymph-nodes, or to the viscera, and does not invade and destroy the surrounding tissues. But attaining to a large size and weight, it becomes exhausting, or, increase in the size of the intra-pelvic portion brings about fatal obstructions, or the occasional rupture of cysts is followed by infection, hemorrhage, ulceration, erysipelas, lymphangitis, and various other complications by which the patient is destroyed.

In a few cases in which the microscopic structure suggests sarcoma, the subsequent behavior of the tumor justified that diagnosis.

PERSISTENCE OF THE OMPHALO-MESENTERIC DUCT

MECKEL'S DIVERTICULUM

If atrophy of that portion of the omphalo-mesenteric duct between the umbilicus and the vitelline loop of the intestine does not follow the usual rule, a vestigial structure remains. It seems to have first been observed by Rysch, but it did not attract much notice until after Meckel published a scientific account of it in 1808, and since then it has been generally known as *Meckel's diverticulum*.

Prior to the third month of embryonal life, the vitelline loop of the intestine makes considerable excursions outside of the abdominal cavity, into the tissues of the developing cord, but during that month, in consequence of the development of the abdominal walls and the completion of the umbilicus, the loop is returned to the abdominal cavity, which closes in front of it. This causes traction upon the vitelline duct, which stretches, ruptures, and finally disappears by atrophy and absorption. But the rapidity with which the last steps take place varies so greatly that anatomists are not agreed about the length of time during which remains of the tissues may persist. Kölliker supposed they

might remain until about the time of birth: Tourneux that they disappeared much earlier. It is certainly not unusual to find traces of the structure in new-born infants, and occasionally they may be found much later in life.

Fig. 109.—Meckel's diverticulum, showing its various appearances. 1. Vitelline loop of the intestine and vitelline canal in an embryo. 2. Vitelline canal, the greater portion of which remains widely open while the narrowed distal end enters the umbilical cord (in a fetus). 3. Vitelline duct, narrowed but still open at the umbilical end and permitting the escape of intestinal contents. 4 Vitelline duct open at the intestinal and umbilical ends, but obliterated in the center, where little remains but a fibrous cord chiefly composed of the obliterated omphalo-mesenteric vessels. (*Lexer.*) 5. Vitelline duct, the distal or umbilical end of which has become obliterated, but still connects with the umbilicus as a fibrous cord. 6. Diverticulum, the distal end of which, detached from the umbilicus, connects with the surface of the intestine, by a fibrous cord, chiefly composed of remnants of the obliterated omphalo-mesenteric vessels. 7. Similar diverticulum attaching to the mesentery in the same manner. 8. Typical free diverticulum of Meckel. 9. Persisting omphalo-mesenteric vessels attaching to the umbilicus without the presence of a diverticulum.

In general the vestiges appear either as slender fibrous bands easily and perhaps frequently mistaken for inflammatory adhesions, or as broad tubular diverticula. Forgue and Riche, who carefully reviewed the subject, give the following tabulation of the malformations of the omphalo-mesenteric duct:
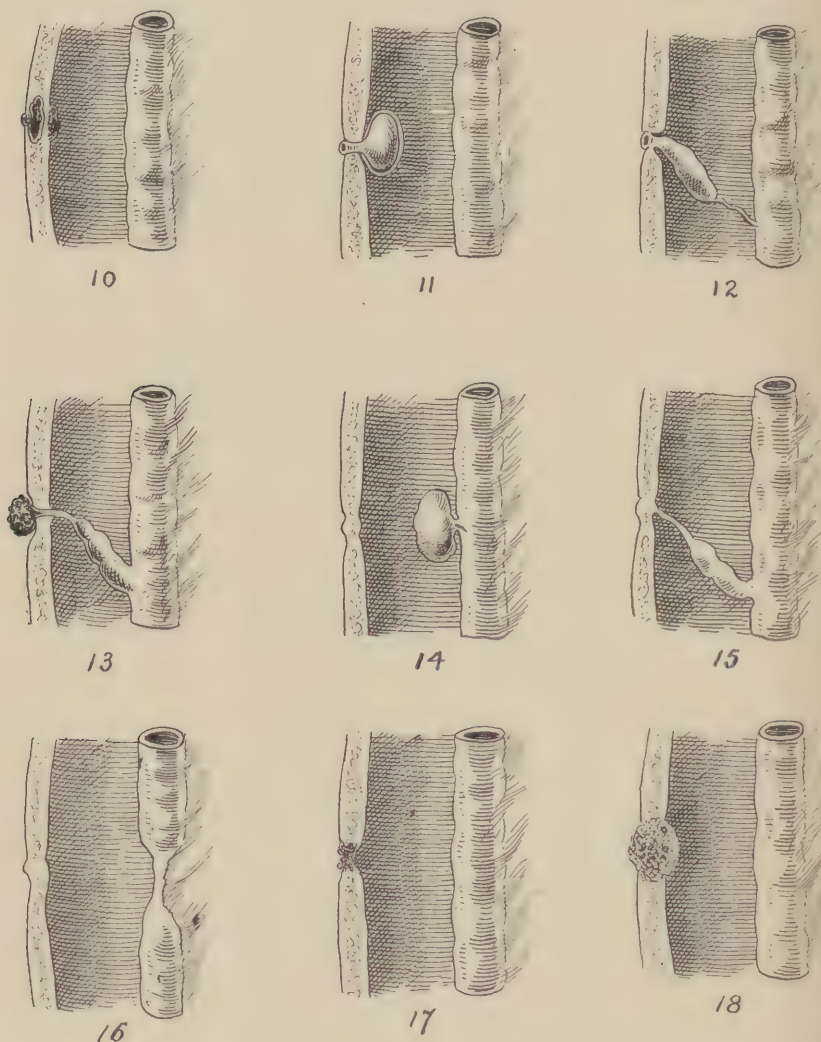
FIG. 110.—10. Intraparietal cyst at the umbilicus, arising from a persisting vestige of the most distal portion of the vitelline duct. (*Zumwinkel.*) 11. Sub-peritoneal cyst at the umbilicus, resulting from the persistence of a vestige of the vitelline duct. (*Roser.*) 12. Cyst at the umbilicus attached to the intestine by a fibrous cord composed of the obliterated inner portion of the vitelline duct. (*Heaton.*) 13. Adenoid tumor of vitelline duct origin coexisting with a diverticulum fixed by a fibrous cord to the umbilicus. 14. Enterocystoma of vitelline origin. 15. Congenital stenosis of the intestine at the point of origin of a diverticulum. (*Bland Sutton.*) 16. Congenital stenosis of the intestine occurring at a point corresponding to the former position of the vitelline duct, and caused by its excessive atrophy. 17. Vitelline or omphalo-mesenteric vestige included at the umbilical cicatrix. 18. Primary cylindrical celled carcinoma, of the intestinal type, of vitelline origin. (*Forgue and Riche.*) (*Redrawn from Forgue.*)

A. Incomplete involution.
    (*a*) Persistence of the connection between the intestine and the umbilicus.
        1. Open diverticulum.
        2. Diverticulum attached to the umbilicus.
        3. Persistence of the omphalo-mesenteric vessels only.
    (*b*) Persistence of the intestinal part of the omphalo-mesenteric duct.
        4. Meckel's diverticulum, either free or secondarily fixed.
    (*c*) Persistence of the umbilical part.
        5. Enterocystomata.
        6. Cysts of the umbilicus.
        7. Residual tumors.
B. Excessive involution.
        8. Stenosis or atresia of the intestine, co-existent with a Meckel's diverticulum.

1. *The Diverticulum is Open.*—In these cases a more or less permeable communication or fistulous passage between the umbilicus and the intestine appears at birth, and permits the escape of either mucous or feces.

Nothing is noticed until the time of the dropping of the cord, when a reddish area resembling an ulceration appears. It is usually bright red in color, about the size of a pea or hazel nut, and sometimes takes the form of a shallow depression, sometimes that of an elevation. Not infrequently this takes the form of a snout, an inch or two in length, and of a red color. Shepherd has reported such a case.

"At the site of the umbilicus was a protrusion which was the size of, and had much the appearance of a child's penis. The projection was 1½ inches long, and had at its extremity an opening which looked much like a preputial orifice. The growth was covered with mucosa, and bled easily. For three or four inches round, the skin was raw, red and exematous. A probe could be introduced into the projection and feces escaped. The fistulous tract was large enough to admit easily a pair of artery forceps."

In more rare cases a pyramidal tumor is seen attached to the umbilical region. If there be no opening, such formations are probably inversions of the mucous membrane of the outer part of a partially obliterated vitelline duct, but if a central opening be present, a probe can usually be introduced into the intestinal cavity. Sutton points out that the appearance presented by the umbilical lesion may depend upon the distance from the umbilicus itself at which the cord was ligated. The greater the length of vitelline duct left behind in the ligation, the greater the length of the protrusion.

The persistent duct, of course, forms a fistula, but what subsequently happens will depend upon its size. If of full size, feces escape, sometimes constantly, sometimes intermittently, sometimes at intervals of two or three days, sometimes only when the child cries or pressure is made upon the abdominal wall. The quantity of matter that escapes is sometimes small, sometimes considerable. When the duct is only partly open there may be a discharge of mucous to which there may be enough admixture of fecal matter to give a characteristic odor. In nearly every case, early prolapse of the mucosa takes place through the external opening, with the resulting raspberry-red colored lesion. How far the prolapse advances will depend in part, at least, upon the size and regularity of the vitelline duct. If it be made unequal at diameter by partial atrophy, only that portion of the mucosa near the external opening may

be able to escape; if it be of full size and uniform diameter, the entire mucous lining may escape, and in some cases may carry with it a considerable length of the intestinal mucosa as well. The resulting appearance varies slightly according to the extent of the prolapse, but is thoroughly characteristic. A tumor appears at the umbilicus, having a dark red color, and a bicornuate or crescentic shape. Some have described it as like the letter T turned upside down, but when very large it may be distinctly sigmoid. When carefully examined it is found to have two openings, one on each horn, or at each end of the S. From one of these, usually the upper, or afferent end of the prolapsed intestine, it is usual to find some fecal matter escaping. The external surface usually shows the characteristic velvety appearance of the intestinal mucosa, caused by its numerous villi, and the valvulae coniventes. It may be possible to reduce the tumor, but early strangulation, deep congestion and swelling, usually make it impossible. The strangulation is quickly followed by gangrene, and with or without operation, the child usually dies in a few days. Of 20 cases collected by Cullen, not one survived. Those that recovered from the shock of the prolapse, either succombed to that of the operation, or died shortly afterwards from pneumonia or some other sequel or complication.

2. *The Diverticulum is Attached to the Umbilicus.*—In these cases the diverticulum does not open externally, and does not show its presence by any external sign. At its intestinal end it is widely open, but at the umbilical end terminates in a kind of cul-de-sac attached to the umbilicus by a fibrous cord.

3. *Persistence of the Omphalo-mesenteric Vessels.*—In these cases the vessels alone extend between the umbilicus and the mesentery. It is very unusual, and Forgue and Riche, in their collection of 650 cases only found it in 2.

4. *Meckel's Diverticulum, either Free or Secondarily Fixed.*—This was found by Forgue and Riche 400 times in their 650 cases of abnormality of these parts. The vitelline canal had lost all connection with the umbilicus, and consisted of an intestinal diverticulum that resembled the finger of a glove, and had about the same diameter as the intestine itself. It was usually free, but was occasionally attached to viscera or different parts of the abdominal interior either immediately or through the intervention of a fibrous filament or cord.

5. *Enterocystomata.*—These were cases in which the intestinal end of the omphalo-mesenteric duct, reduced to a vestige imbedded in the intestinal wall, and not always having a communication with the intestinal lumen, underwent cystic dilatation, appearing as a cystic tumor.

6. *Cysts of the Umbilicus.*—Here the reverse is observed. All of the vitelline duct except the merest vestige at the umbilical end has disappeared, and the residuum is imbedded in the abdominal wall, either partly or completely. Subsequent cystic dilatation results in a tumor at the umbilicus.

7. *Residual Tumors of the Umbilicus.*—The only difference between these and the former is that they are solid instead of cystic tumors.

8. *Stenosis of the Intestine.*—In regard to the excessive involution of the omphalo-mesenteric duct, Forgue and Riche agree with J. Bland Sutton that obliteration does not always stop at its point of insertion into the intestine, but sometimes continues beyond the normal limits, so as to include a part of the wall

of the intestine itself, giving rise to a deep groove resembling an intestinal diaphragm with a central opening. The intestine may even be divided into two portions connected by a very narrow pervious cord, or of two portions entirely separated from one another.

Care must be taken not to confuse Meckel's with other forms of intestinal diverticula. It arises above the ileo-caecal valve, but the exact point varies. Wernher once found it only 3 cm. above the valve, and Rolleston once 3 metres above it. Forgue and Riche found its average distance from the valve to be 68 cm. It is, however, always in connection with the ileum, and it always arises from its convex surface and at right angles. Its wall includes all of the intestinal coats. It is single.

False diverticula, are commonly multiple, occur anywhere along the course of the intestine, and usually have only the mucous and serous coats of the intestine.

The frequency with which Meckel's diverticulum occurs varies greatly according to different writers. Aschoff states that it occurs in 2% of autopsies. Balfour found that of 10,600 laparotomies at the Mayo Clinic, it was observed only 15 times. Keen found it more frequent in men than in women, the proportions being given as 100:30.

Its length is also subject to variation, 2 cm. being given as the mean and 25 cm. as the extreme length. Its diameter is almost always about the same as that of the intestine itself. In most cases it terminates in a rounded extremity like the finger of a glove, but it may end in a long slender filament, free, or attached either primarily at the umbilicus, or secondarily to some other part of the abdominal interior. When it is filamentous it may be hollow or solid, either for all or a part of its length. The larger diverticula have anatomical and histological structure perfectly corresponding with the intestine itself, even including the patches of Peyer. But when the diverticulum is reduced to a slender cord, its structure is principally fibrous.

In general, Meckel's diverticulum is a harmless embryonal survival, as might be suspected from the great number of cases in which it is first discovered at autopsy. But it can be troublesome, and may cause death. Hence it is advised by many of the best surgeons, that if the abdominal cavity of a patient be opened for any cause, and a Meckel's diverticulum found, it be removed.

The chief complications that may result from its presence are:

I. *Intestinal Obstruction.*—In these cases the part played by the diverticulum may be either active or passive. The following tabulation of the obstructions is taken from Forgue:

I. Malposition

A. *Invagination.*—The diverticulum turns upon itself like the finger of a glove, in such manner that its cavity is delimited by the peritoneal surface, and may also penetrate into the ileum. Of such cases there are three degrees:

1. The diverticulum is simply invaginated into the ileum.
2. It carries with it the afferent loop.
3. The invagination reaches and passes through the ileo-caecal valve.
    In such a case seen by O'Connor, a fragment of the intussusceptum sloughed off and was passed in the stools.

B. *Volvulus.*—This is torsion of the diverticulum upon its long axis, with one, two, or three turns, affecting the lumen, and causing serious circulatory disturbance of its walls. The process may affect the diverticulum alone, or the intestine simultaneously. Gangrene and peritonitis usually quickly follow, with or without perforation. Volvulus may occur either in free or fixed diverticula.

In the case reported by the author in 1901, the patient died of obstruction of the bowels caused by combined volvulus and invagination of a Meckel's diverticulum that arose about 60 cm. above the ileo-caecal valve, was about 4 cm. in length when straightened out, and had undergone a corkscrew twist equal to one complete turn on its long axis, and then invaginated itself so as to project into the lumen of the bowel where its swollen tissue caused a firm obstructing node.

C. *Torsion of the Intestine.* Twisting of the intestine upon its long axis may occur in consequence of the weight and swaying of a diverticulum partly filled with fecal matter. In some cases there may be torsion of the intestine about the axis of its mesentery.

D. *Flexure of the Intestine.* The intestine may be bent over a diverticulum fixed to the umbilicus, and held down on each side by the weight of its contents so that the lumen is closed. Or, the band may press upon the intestine and close its lumen.

II. Compression

A free diverticulum sometimes twists about the intestinal loops and may even tie itself into complete knots, as in cases reported by Parisi, and by Borden. Such compression is more rare, however, than in cases in which the intestine gets caught under bands of tissue representing vestiges of the vitelline duct. When derived from the vitelline vessels such bands sometimes form a kind of ring through which the loop of intestine passes. Such formations are always congenital.

III. Obstructions

These are supposed to result from vicious positions.

IV. Stenosis

These are not rare, and are congenital in all cases.

Obstructions resulting from any of the causes tabulated usually develop acutely, and only rarely can it be determined that the patient has had previous trouble with the intestines. There is nothing about the symptoms sufficiently characteristic to enable the diagnosis to be correctly made. According to Fritz, only about 5% of the intestinal obstructions are referable to Meckel's diverticulum. The patients are nearly always young adults, 75% of them are less than 30 years of age, and most of them are males. If not relieved by surgical operation, most cases die between the fourth and eighth days.

Meckel's diverticulum has a well developed muscular coat through the contraction of which contents may be expelled. But nevertheless, matter sometimes accumulates in diverticula, and may excite inflammation or open the door to infection. Hagler and Stewart have reported a case of perforation of a Meckel's diverticulum by a fish bone. The diverticulum may also be injured by impacted feces or foreign bodies, and either may inflame, suppurate, become gangrenous, and eventually perforate.

II. *Intestinal Perforation.*—This sometimes results from typhoid ulcerations as in cases reported by Halstead, Cattell, Galton, Bonetin and others, or from tuberculous ulcerations, as in the cases reported by Fitz, Dixon and Antonelli.

It is impossible to foretell the consequences of perforation. Sometimes it results in a circumscribed, well walled-off abscess, sometimes in generalized peritonitis.

III. *Hernia.*—This is the third chief danger arising from the presence of Meckel's diverticulum. Hernia does not occur because the diverticulum is itself the cause, but because it is more easy for it than the intestine proper to slip into a hernial opening. This seems to have been first pointed out by Ruysch, though little attention was paid to it until 1700 when Littré carefully studied the matter. And since his time such hernias have been called Littré's hernias.

FIG. 111.—Meckel's diverticulum as it usually appears. One-fourth natural size. (*Photograph by Prof. Allen J. Smith.*)

Such hernias occur in the inguinal, femoral and umbilical regions, sometimes forming the entire contents, sometimes in association with other portions of the intestine, and behaving as the other portions of the intestine do. That is to say, the diverticulum may become incarcerated, inflamed, adherent, strangulated, etc. As its presence confers no particular quality upon the hernia, there is no way by which its presence can be discovered, either through physical signs or symptoms.

The vestiges of the vitelline duct included in the abdominal or intestinal walls, may form tumor-like masses, or actual tumors, though conforming to no recognized type of tumor structure, and having no place in the ordinary systems of classification.

Those arising from the intestinal segment, may be either attached to, or included in the intestinal wall, and are therefore usually spoken of as intestinal tumors, and generally as *enterocystoceles*. They are usually observed in young females.

Such a tumor may grow larger in such a manner as to obstruct the intestine and suspicion that malignant change may occur is usually expressed, though there seems to be very little foundation for it.

The vestiges remaining at the umbilical end also give rise to both cysts and tumors, which may be sub-peritoneal, intra-parietal, or sub-cutaneous in position, and large enough to attract attention at once, or so small, concealed and unobtrusive as to escape attention until years after birth. The most frequent form assumed is a cystic tumor in which are epithelial spaces lined mucous membrane resembling that of some part of the alimentary canal. The more solid tumors resemble adenoma, and, indeed have been described as such by Lannelongue and Trimont. Most of them fall into the group that Cullen

in his interesting book, "The Umbilicus and Its Diseases," describes as *polypi*, —that is, small raspberry-like, red, bleeding elevations that usually make their appearance at the time that the cord separates, as the result of prolapse of the mucosa from the distal end. Their formation seems to depend upon the fact that the outer part of the vitelline duct remaining open, inverts, so that the fibro-muscular wall is on the inside, and the mucous membrane on the outside, giving the polyp its red color. These formations are very annoying because of their tenderness, discharge, and tendency to bleed upon slight provocation, though they otherwise do no harm, even when, as has sometimes been the case, they have been allowed to go untreated for years. In the case reported by Hartmann, the patient was 29 years old. In one case reported by Kirmisson the tumor was composed of three lobes, but no significance is attached to the shape, and the etiology of the tumor was the same.

When the polyp is examined microscopically, it is sometimes found to be covered with what resembles gastric mucosa. It must not be inferred from this that it has any connection with the stomach, or is in any way derived from it. As Cullen points out, the entire alimentary canal is developed from the embryonal yolk sac, and all parts of it are said to be very much alike in appearance until changed by contact with the gastric, hepatic and pancreatic fluids.

The possible embryonal inclusions, displacements, malformations and compensations about the umbilicus furnish almost unlimited opportunity for tumor formation later on. Myxoma, may grow from vestiges of the substance of the cord; lipoma from adipose tissue entering the loosely closed umbilical opening from the subjacent sub-peritoneal tissue, as is quite common in hernia; myoma from vestiges of the muscular coat of the vitelline duct; carcinoma of cylindrical cell type from the epithelial lining of the duct, and of the squamous cell variety from the squamous epithelium of the skin.

An exceptionally interesting muscular tumor of the umbilical region is the adeno-myoma, a tumor composed of unstriated muscle in which are epithelial glands embedded in a delicate fibrillar tissue stroma. These are believed, by Cullen, to be derived from vestiges of the ducts of Müller as the microscopical identity of their tissue with that of the uterus seems to be undoubted. One may ask how vestiges of the ducts of Müller can possibly be caught in the tissues of the umbilicus, and the only answer seems to be the general propinquity of the tissues during the early stages of development—not a very satisfactory explanation.

But, "it is clearly seen that the gland picture is that of the uterine mucosa, with its typical glands and its characteristic stroma, and further that the typical menstrual reaction is often present as evidenced by pain in the nodule at the periods, and accumulation of old menstrual blood with the formation of small cysts, and in at least one instance, by the occasional discharge of blood from the umbilicus. In this case one or two glands opened directly upon the surface, thus allowing free escape of menstrual blood. In all, nine cases have been recorded. . . we have in this group of cases, glandular elements that from their histological appearance and arrangement correspond exactly with those in adeno-myoma of the uterus, and in one case at least, the surrounding stroma was composed chiefly of non-striated muscle, making the growth essentially an adeno-myoma. In the majority of the cases, however, the stroma consisted of fibrous tissue, but little muscle being present."

Sarcomas of various types have been observed to arise at the umbilicus. Their relation to the embryonal vestiges needs no emphasis.

PERSISTENCE OF THE URACHUS

As the bladder develops, the part of the allantois above it, forming the communication between it and the umbilicus, is called the *urachus*.

During the third month of embryonal life this begins to atrophy, first losing its permeability, then undergoing fibrous transformation, until at the time of birth nothing remains but a slender cord passing from the fundus of the bladder to the umbilicus between the peritoneum and abdominal wall. If transverse sections are made of various parts, it is not unusual to find that the obliteration has progressed irregularly so that here and there collections of epithelial cells, and even occasional epithelial lined spaces remain. These were first observed by Luschka, and are usually called after him, *Luschka's lacunae*.

Wurtz found that in 69% of 74 cadavers studied, a minute canal, into which a horse-hair could be introduced a distance varying from 2 to 4 mm., passed from the fundus of the bladder in a direction corresponding to that of the urachus. Couget examined 82 cadavers of new-born infants, and found the urachus patulous in two. Such vestiges of the urachus as are observed in post-natal life, ascend the abdominal wall between the peritoneum and the muscles. Sometimes they can scarcely be seen, sometimes they form a considerable ridge, and may even appear as cord-like structures separated from the abdominal wall by a mesentery-like peritoneal fold.

It is difficult to make accurate observations upon urachal vestiges. If they are to be studied, and their permeability judged by the introduction of a probe, the irregularity and unequal diameter of the canal makes its passage difficult; if the attempt is made to do so through the injection of fluids, valvular folds in the membranous lining interrupt its course. If studied by transverse sections, obliteration of parts of the canal gives a false impression regarding the whole.

Occasionally it turns out that there is a pervious urachus where it was in no wise suspected, and might never have been detected had not circumstance brought it to light. Such cases, becoming the victims of enlargement of the prostate gland or of stricture of the urethra, assist the force of micturition by compressing the abdomen. To their surprise the urine not only escapes from the urethra, but also from the umbilicus. There is a theory that patulous urachus occurs only where there had been antecedent urinary obstruction, and such cases are sometimes adduced in support of it. However, in the cases mentioned the urinary obstruction comes late in life, and without the least suspicion of any early similar trouble. But the fact that there is such a theory, and that there are such cases as have been described, indicate that before any case of urachal fistula be operated upon, the surgeon would do well to investigate and see whether there be any urinary obstruction to which the appearance of the fistula is secondary.

Complete permeability of the urachus, and consequent urinary fistula is very rare, and is characterized by the escape of urine through both the urethra and the umbilicus during urination. It is much more frequent in males than

in females, probably because of the greater complexity of their urinary passages. Of 53 cases collected by Cullen, 35 were in males, and 18 females.

In some cases with persisting urachus the appearance of the umbilicus is normal; in others there are peculiar fleshy formations. In a case reported by Lannelongue, the mother of the child consulted the physician because she thought her little boy had two penes, one in the normal position, the other at the umbilicus. It turned out, that in that particular case, there was also an umbilical hernia, but the same appearance may occur where there is none, as in case reported by Mayer. But far more common is the occurrence at the umbilicus of a little firm, red or purple nodule varying in size from a pea to a cherry, and sometimes said to resemble a strawberry. In a case reported by Alric the tumor is said to have measured 3–4 cm. in diameter, and to have been bright red. In one reported by Cabrol, it is said to have resembled the comb of a turkey-cock.

The external orifice of the fistula is usually very small, and sometimes will scarcely admit the finest probe; at other times it is large enough to admit a large catheter. There seem to be no cases in which the vestigial urachus had an external opening only. But such might well have escaped observation as with a small lumen, the quantity of discharge would be very small, and with no communication with the bladder, its character would be inoffensive, and the moisture discovered by the patient attributed to perspiration.

On the other hand there are many cases in which there has been an internal orifice only, and it has already been pointed out that a minute canal, into which a fine probe could be introduced not infrequently arises from the fundus of the bladder at the point corresponding with the vesical end of the urachus.

If the wall of such a vestigial canal is sufficient to withstand the intra-vesical pressure, no change may occur, but if it be a little weaker, or the intra-vesical pressure augment, the vestigial canal may dilate and lead to the formation of a diverticulum. With free communication between the bladder and the diverticulum, so that the latter empties as soon as the contraction of the former are at an end, no further result than gradual enlargement of the diverticulum may accrue, but should the communication be such that, with each effort at urination, the urine is forced in, but escapes with difficulty, a more rapid and greater diverticulation becomes possible. Further, a certain quantity of stagnant urine in which calculi may form may remain, and cases have been known in which they have not only formed, but have subsequently ulcerated through the suprajacent tissues and escaped from the body, leaving a fistulous tract.

There are also cases in which both the internal and external ends of the urachus have been closed, but leaving the Luschka's lacunae. Here again nothing may happen, or for reasons not understood, exudation may occur into the spaces, and cysts form.

Small and large cysts of the urachus are described. Small cysts are only about a centimeter in diameter, are rather frequent, but are nearly always discovered accidentally, either in the course of surgical operations, or at autopsy.

The large cysts may attain to a very large size. The largest upon record seems to have been reported by Rippmann. It filled the abdomen and contained 52 litres of fluid. Another reported by Freer, contained 50 litres. One removed

by Lawson Tait contained 17 litres. A large number of cysts the size of coco-nuts or oranges are on record.

Weiser in 1906 was only able to collect 86 cases of the large cysts, some of which were probably not authentic. In the same year, 1906, Delore and Cotte reported two new cases and collected ten, all of which were undoubtedly authentic. In Cullen's book upon "Diseases of the Umbilicus," 21 cases are collected from the literature. Large cysts of the urachus are much more frequent in women than in men, the proportions given by Cullen being 16 to 5. The youngest patient was 6 years of age, the oldest 54. The greatest number of cases occurred between the 30th and 50th years of life. In a case observed by Cullen and Welch, the cyst occurred in association with a tumor, a neuroma, of the wall of the bladder.

The walls of the cysts consist of fibrous connective tissue, with more or less admixture of unstriated muscle, and they are lined with the stratified squamous epithelium of the urinary tract. In no case has any other variety of epithelium been found.

The contents are serous, for the most part much like ascitic fluid, the exact composition varying according to the quantity of colloids rather than of other ingredients. There is never any urine. If a collection of urine is found, it is not a cyst, but in a diverticulum with a narrow entrance.

Tumors, both sarcoma and carcinoma have been reported as arising from urachal vestiges, but are extremely rare.

Retro-vesical Cysts

Small cysts rarely observed upon the posterior wall of the bladder not far from its neck, have a very different origin and presumably are derived from vestiges to Müller's tubes. They are very rare, usually very small, and have no surgical significance.

PERSISTENCE OF PFLÜGER'S TUBES IN THE OVARY

Ovarian Cyst and Cystoma

The first appearance of the sex glands, in both the male and female, is said by McMurrich to take the form of the genital ridge. From various authorities the subsequent events are described as follows:

The first indication of the formation of the genital ridge is the assumption of a high columnar form by the epithelial cells of the upper part of the mesial surface of the Wolffian ridge, and shortly after this thickening has appeared, a condensation of the underlying mesenchyme occurs. At first the ridge is of insignificant dimensions compared with the more voluminous Wolffian body, but as the degeneration of the latter proceeds the relative size of the two structures becomes reversed, and the genital ridge forms a marked prominence attached to the surface of the Wolffian ridge by a fold of peritoneum which becomes the mesovarium in the female, and the mesorchium in the male.

The sex gland at this early stage cannot correctly be assigned to either sex, and is therefore described as the *indifferent sex gland*. It is formed during the fifth week of embryonal life through the thickening of the mesothelial elements to which Waldeyer gave the name *germinal epithelium*, because after the development of the sex glands proper, they furnished the super-matozoa or ovules respectively according to the sex of the individual.

The transformation of the indifferent sex gland into the ovary is simple to follow. The germinal cells collect upon its surface at the time that the mesothelial tissue is thickening to form the organ proper, and by the sixth or seventh week consist of several strata which begin to penetrate the underlying mesenchyme in the form of cords or egg-columns—the Pflüger's tubes. Each contains two kinds of cells, the larger germinal cells or primitive ova, and more numerous smaller cells of the mesothelium. The egg-columns, with the surrounding young connective tissue, constitute the cortex of the future ovary. It is sharply marked off from the free or peritoneal aspect of the gland, the region of the germinal epithelium, by a zone of proliferating mesodermal cells which become the tunica albuginea of the ovary. The egg-columns later become broken up, so that each germinal cell is separated from its fellows, and surrounded by a group of smaller cells. These are the Gräffian follicles. The enveloping zone of connective tissue becomes the theca folliculi; the smaller cells the membrana granulosa, and the germinal cell the ovum. The subsequent formation of new ova and Gräffian follicles begins in the deeper part of the ovary and advances to the surface. Their production is, however, limited to the fetal stage, and early part of post-natal life, none being found, according to Waldeyer, after the second year. The medulla of the ovary is produced by the growth of cord-like medullary processes—the medullary cords—from the epithelial walls of the Malpighian corpuscles of the primitive kidney or Wolffian body, the cords being surrounded by connective tissue and forming a net-work. The fetal medullary cords are represented in both the cortex and medulla of the mature ovary by groups of interstitial cells disposed between the bundles of the stromal tissue. Except for these medullary cords, the Wolffian body plays no part in the formation of the ovary, and it as well as the Wolffian duct, entirely disappears by atrophy.

Histologists generally seem to follow Waldeyer in the belief that in human beings the formation of Gräffian follicles through the activity of Pflüger's tubes is completed soon after birth. But the matter is by no means certain. In some of the lower animals it goes on continuously during the entire life of the creature, and it may continue for years in human beings, as occasional Pflüger's tubes are found in the mature ovary.

The number and variety of cysts and cystic tumors of the ovary is bewildering, and classifications of them numerous. No general consensus of opinion in regard to their origin and nature has yet been reached. For this reason an author is free to express any opinion that seems best able to explain what he finds.

But before proceeding with the explanation, it may be well to examine and see what is to be explained.

One of the most frequent morbid growths of the ovary is that known as the *cystoma* or *cystadenoma*. It is of variable appearance, and figures under several sub-headings, as

1. Cystadenoma Simplex
2. Cystadenoma Papilliferum
3. Superficial Papilloma.

Supposing that the varieties are but conditions, the tumor sometimes appears nearly or quite solid, sometimes as a single cyst, sometimes as a congeries of cysts, sometimes as a spongy growth made up of innumerable large and small cysts. Forgue divides them into:

1. Unilocular cysts
2. Paucilocular cysts
3. Multilocular cysts, or cystic tumors.

He also speaks of them as mucous cysts to clearly separate them from the dermoid cysts. They are also frequently called *pseudo-mucin cysts*, because their spaces are commonly filled with a viscid gelatinous material, pseudo-mucin, a protein of complicated composition differing from ordinary mucus in tending to reduce Fehling's solution with the production of a red color.

The tumors are nearly always unilateral. They vary up to the almost unbelievable size of 50 kilogrammes. They occur in adults of almost all ages and Kelley, Wiel, and McGillevray have seen them in children. They are rounded or ovoid in shape, usually smooth, though sometimes nodular or bosselated on the surface which may be covered with shining peritoneum, or roughened from torn adhesions. Parts of their substance may be firm, parts soft and fluctuating. In some, the external surface is partly covered by dendritic papillary excrescences. When sectioned, a single large cavity, a number of small cavities, or some large and innumerable small and minute cavities filled with differing contents may be discovered.

In some cases it is clear fluid not unlike acitic fluid; in others clear, amber colored, and viscid; in still others thick bluish or yellowish jelly. In some cases the contents are modified by the addition of varying quantities of blood, making them red and opaque if recent, or dark red and transparent if older or of pus or necrotic amorphus matter, giving them a whitish or grayish opacity.

The outer wall of the tumor is usually made up of dense fibrillar connective tissue, but the partitions between the cysts themselves are more commonly soft and spongy, being made porous through the presence of great numbers of minute cysts. The walls of the cavities may be perfectly smooth, or partly smooth, and from the inner surfaces single or multiple papillary excrescences of dendritic form may arise. In the large cysts these are usually few, but in some of the smaller ones they are so numerous as to fill the space and transform it into what appears to be a solid structure. In regard to these papillae care must be exerted not to mistake wrinkles and folds of the lining epithelium for actual excrescences. Parts of the walls are sometimes dense and calcified, and may contain fragments of bone. Not infrequently they show numbers of chalcospheres or psammoma bodies. Occasionally they are complicated by the unexpected presence of dermoid cysts. With these they probably have nothing in particular to do, the cystoma having grown about a pre-existing dermoid, or a germinal cell caught in its substance later developing into the dermoid.

The walls of the cysts are lined with a single layer of beautiful columnar epithelium. Only in the rarest cases do the cells pile up in several layers. The cells, however, differ in different cases. They are usually of a high cylindrical shape, but in the large cysts may be flattened. Usually they are uniform, but occasionally they show more or less numerous goblet cells. One of the most interesting features is the presence of ciliated cells. The number and distribution of these varies. In rare cases all of the cells are ciliated; in a greater number of cases many of the cells are ciliated, or all of the cells in some particular cyst are ciliated; in other cases only a part of a cyst wall will show ciliated cells.

To the naked eye the cyst walls are sometimes smooth and shining, sometimes dull, porous, or even roughened and uneven. Smoothness usually depends

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upon simplicity of microscopic structure, roughness upon complexity, the cyst wall in the latter case being filled with gland-like pockets and depressions.

The multilocular cysts rarely communicate. There is, however, plenty of evidence to show that their partition walls frequently become attenuated and rupture, bringing neighboring cysts into communication, and leaving the stumps of the partitions sticking out like dendritic excrescences into the cavity, especially when their collapse and atrophy are retarded through calcification or osseous transformation.

When the cysts are superficial and the walls thin, they sometimes rupture externally, the contents escaping into the peritoneal cavity, where it diffuses when serous, or floats in flocculi or collects in recesses according to its density and tenacity. Following the rupture of the cysts excrescences frequently develop upon the surface, and later attach to neighboring structures, or, detached cells or bits of the papillary excrescenses may implant into them, and cause the appearance of secondary papillary growths.

If an ovarian cystoma is smooth on the surface and without adhesions its removal is easy and it does not return. If it is rough on the surface and adherent, it is difficult to remove and there may be returns from imbedded papillary processes. Most ovarian cystomas are benign. About 30%, and mostly those with papillary excrescences are malignant. It is said that, in some cases, the removal of the primary growth is followed by the spontaneous disappearance of the auxiliary growths.

From this description it seems that, although there are considerable differences in the appearances of different cysts, they are intimately related. Cruveilhier attempted to classify them through the differences in their contents, but eventually gave it up saying that "from the unilocular and paucilocular serous cysts to the complex cystic masses with the formation of areolar and gelatiniform tissue, it was possible to find all the anatomical transitions."

This merging of the different varieties into one another is important to keep in mind when the origin of the cysts is sought for. The origin of all may be the same.

From what elements of the ovarian structure can these tumors arise? Not from the stroma, of course, for the most striking and important elements are epithelial. Of epithelial elements there are many to choose from. There is first of all the germinal epithelium of the surface; second, the Pflüger's tubes or cellular prolongations by which the germinal epithelial cells are carried into the depths of the ovarian cortex; third, the germinal cells themselves; fourth, the cells of the stratum granulosum of the Gräffian follicle. To these must be added the vestiges of the tubules of the Wolffian body—the epoöphoron—that Nagel, von Recklinghausen and Franqué have shown sometimes to be included in the tissues of the ovary. Lastly there may be occasionally inclusions of groups of the surface epithelium which Waldeyer observed and thought might be the source of the goblet-cell cysts of the cyst-adenoma.

Each of these has been suspected, and each has the backing of influential names in support of its probable importance. It is not by any means certain that each may not be responsible for some cystic tumor or tumors, but nothing

has been or at present can be proven. In the absence of positive information, each may choose for himself. It seems to us that the Pflüger's tubes merit most serious attention as the probable source of the tumors because from a certain point of view, the development of a cystic tumor in the ovary seems to be little more than an exaggeration of the normal conduct of these structures. But they are supposed by Waldeyer and most histologists to complete their function and disappear by the second month of postnatal life. It is not certain, however, that they do, and even so there may be persistence of some of them, and to this occasional persistence and the results that follow in its wake, it seems most satisfactory to attribute the origin of most of the cystic tumors of the ovary.

Suppose the cell masses and strands with the "egg-balls" of Waldeyer, that collectively seem to be included in the general term Pflüger's tube, and whose function it is to form Gräffian follicles, in part survive, and retain their primary function or a modification of it. Then at any time may begin the multiplication of cells, the formation of pockets analogous to the follicles, the secretion of fluid, and the formation of cysts. According to the vegetative energy of the residual elements there may be a single pocket, unilocular cyst; several pockets, pauciloc-ular cysts; or many pockets, multilocular cysts. The columnar cells lining the pockets are derived from the same source as those of the stratum granulosum of the Gräffian follicle; the fluid of the cyst is primarily the secretion of these cells, subsequently augmented by exudation. Pseudo-mucin is subsequently super-added as the result of secretion by the cells, and degeneration of the tissue. The occurrence of ciliated cells is in no manner opposed to this theory, because the cells of the stratum granulosum are known, since the work of von Velitz to occasionally be ciliated—in fact, ciliated epithelium can descend from any of the cell sources to which the origin of the cysts could be ascribed, so that its presence or absence neither supports nor detracts from any theory. The papil-lary excrescences are partly the result of the survival of partitions intermediate between cysts that have coalesced through the rupture of the partitions; partly due to the wrinkling and folding of the epithelial lining with accentuation of those parts best vascularized and decadence of others. The appearance of the excres-cences upon the outer surface of the cysts or upon the outer surface of the ovary itself is either the result of the rupture of superficial cysts, portions of whose partition walls survive, or, as in the interiors of the cysts themselves, from the described wrinkling and folding of the epithelial membrane with excessive develop-ment of the better vascularized portions.

Thus nearly all of the characteristic features of the cystoma can be accounted for through this theory which has in its support the names of Klebs and Wal-deyer, Wilson Fox, Pfannenstiel, Gebhard and others.

But the cells of the Pflüger's tubes are after all the descendents of the germinal epithelium of the surface of the ovary, and some, among whom are Malassez, de Sinety, Flaischlen and Coblenz, thinking that they have traced connections between the cells of the surface and those of the interior, prefer to think that the tumors are derived from the former.

Marchand and von Velitz held a different opinion, and thought that the cells of the stratum granulosum were the starting point of the tumor.

Nagel, von Recklinghausen, Bandler and others inclined to the belief that it was derived from vestiges of the tubules of the Wolffian body.

PERSISTING VESTIGES OF THE WOLFFIAN BODY

In the Female

All that remains of the mesonephros or Wolffian body, in the female, is a group of ten or fifteen parallel tubules situated between the two layers of the
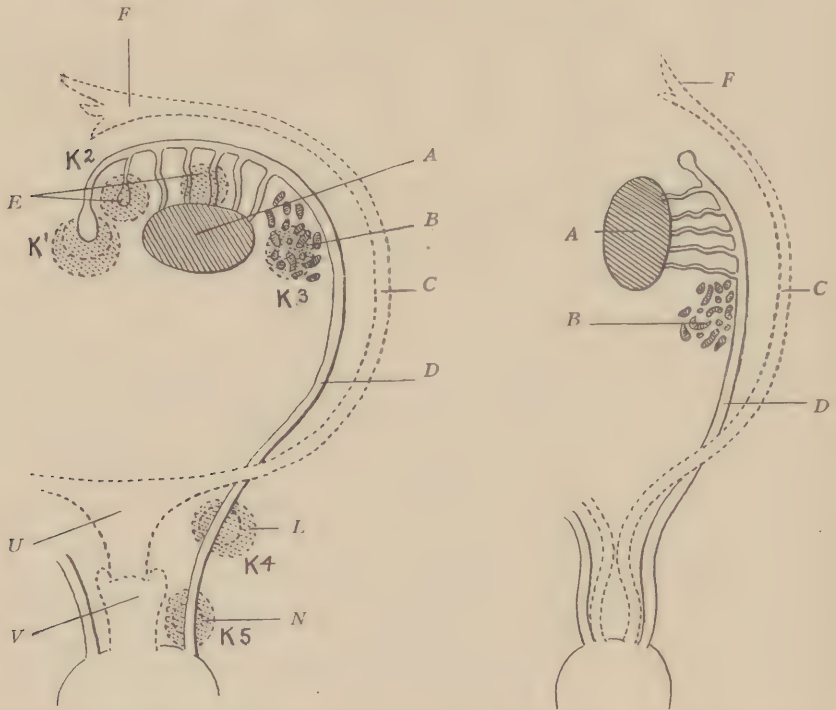
Fig. 112.—Diagrams showing the origin and position of the various cysts derived from the Wolffian body and duct. (*Redrawn from Forgue.*)

A. Ovary. *B*, Parovarium. *C*, Duct of Müller. *D*, Wolffian duct. *E*, Cysts of the body of Rosenmüller. *F*, Infundibulum of the duct of Müller. *U*, Uterus. *V*, Vagina. K_1, The hydatid Morgagni. K_2, Cysts of the body of Rosenmüller. K_3, Cyst of the Parovarium. K_4, Cyst of the uterine portion of Gärtner's duct. K_5, Cyst of the vaginal portion of Gärtner's duct.

broad ligament, in close proximity to the ovary, and constituting the *parovarium* or *organ of Rosenmüller*.

The tubules comprising this structure are usually blind at both extremities, but in exceptional cases connect at one end with a larger vestigial tube at right angles to them—the Wolffian duct. All of these are lined with tall columnar epithelium sometimes provided with cilia.

From these various vestiges cysts sometimes arise, and may be recognized by a few usually well marked characteristics:

1. They arise between the layers of the broad ligament.
2. They are usually unilocular.
3. The walls are usually very thin.
4. The contents is a thin transparent watery fluid.

So long as such cysts remain small enough to be contained between the layers of the broad ligament, there ought to be very little difficulty in determining their origin, but as they grow, they ascend, tend to disengage themselves from their original position, and may hang by a pedicle of considerable length, and always of considerable breadth, formed at the expense of the broad ligament. The Fallopian tube of the affected side is drawn out over the surface of the cyst, sometimes for half of its circumference, and the fimbriae, widely separated, are stretched some distance further.

The wall of the cyst is, as a rule, very thin, consisting of a layer of connective tissue the outer surface of which is covered with a serous layer derived from the peritoneum, and the inner, lined with columnar epithelium, which not infrequently shows cilia in well preserved specimens.

The cells are not always uniform in type, however, so that in making microscopic studies, several different parts of the cyst wall should be cut for examination. It may then be found that one portion shows the typical columnar form, another cuboidal cells, and a third, perhaps, flattened cells. If, as is most frequently the case, the cyst spring from a single tubule, it will be unilocular; if from two or more tubules, paucilocular; if from the whole series, multilocular. But other than unilocular cysts are marked exceptions and there are never any cystic growths at all comparable to the ovarian cystoma.

Small warty vegetations are occasionally seen upon the inner walls of the cysts.

The cysts are nearly always filled with clear watery fluid that contains so little protein that it usually does not coagulate upon boiling. This is one of the most characteristic and constant features of the parovarian cysts, but also has its exceptions. Occasional cysts have viscid contents, especially when they show excrescences upon their inner walls.

In the Male

The testis and epididymis are occasionally provided with minute appendages supposed to be vestigial survivals of the Wolffian body. They comprise:

1. *The Appendages of the Rete Testis.*—These first described by Roth and Poirier, comprise a few blind tubules that extend into the lower end of the globus major from the testis, and lie buried in the former or project as small elevations upon its free surface. They are supposed to be tubules of the Wolffian body that have lost connection with the canal of the epididymis—Wolffian duct.

2. *The Appendix Epididymis.*—This is also known as the "stalked hydatid," and is a small pyriform body 3 to 4 mm. in greatest diameter, attached to the upper pole of the globus major of the epididymis. It is variable in size, and there may be two or more. The origin is a little uncertain, and some think it derived from the Müllerian duct.

3. *The Paradidymi.*—Ordinarily a single structure is described as the paradidymis or organ
of Giraldes, but according to Toldt there are two which he calls the upper and the
lower.

The *Upper Paradidymis* or organ of Giraldes is composed of an irregular group of blind
tubules 5 to 6 mm. in extent, lying in the lower end of the spermatic cord, above but
close to the globus major of the epididymis, always in front of the venous plexus. It
is the homologue of the paroöpharon of the female, is inconstant, and usually dis-
appears in early childhood.

The *Lower Paradidymis* is composed of a single coiled tube that lies behind the globus
major of the epididymis, in front of the veins. "It may be isolated, connected with the

FIG. 113.—The sac of a hydrocele of the tunica vaginalis, laid open. On the posterior
wall, the testis and epididymis are seen projecting into the cavity, with the "hydatid of
Morgagni" on the epididymis. (*Bowlby and Andrewes.*)

canal of the epididymis, with the rete testis or with both, these varying relations
being explained by its probable source as an efferent duct that has become completely
or partly disconnected. This tube is frequently the seat of cysts which, when the
canal retains its connection with the epididymis or testis may contain spermatozoa."

4. *The Vasa Aberrantia,* or the vasa of Haller. These consist of one or two blind tubules
which arise from the tail of the epididymis near the beginning of the vas deferens, and
extend for a varying distance into its tissues. When there are two, the upper, usually
the shorter, attached to the rete testis, pursues a downward course in the epididymis,
while the lower and usually larger sometimes having a length of 30 cm. passes upward
from the lower part of the canal of the epididymis. There may be several such con-
voluted tubules.

From any of these vestigial structures cysts may arise, and indeed it is chiefly
because of a slight cystic distension that some of them are usually detected.
Though their positions, as described, seem to be well defined so soon as they

develop into fair sized cysts the relations are lost and it becomes increasingly difficult to recognize them. On this account it is more frequently the custom to classify the cysts of this region clinically than pathologically or etiologically. Thus, Gosselin thought it sufficient to divide them into:

     1. Small cysts without spermatozoa
     2. Large cysts with spermatozoa.
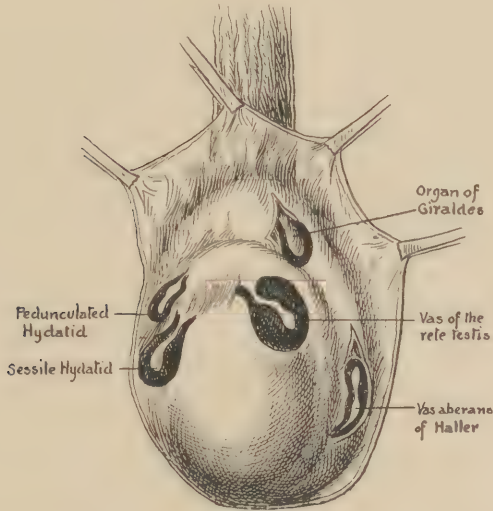
FIG. 114.—Diagram indicating the position and origin of the small cysts occurring in connection with the testis. (*Redrawn from Forgue.*)

But this is in no sense adequate, nor is it satisfactory. The small cysts may at any time grow larger if let be, and the larger ones were all once small. Moreover, cysts without spermatozoa may at any time begin to contain them through abnormal communications resulting from secondary changes. Unfortunately there seem to be neither anatomical nor histological characteristics upon which the cysts can be separated. They all have the same general structure, and consist of a very thin fibrous tissue wall with a single layer of columnar or cuboidal epithelium.

In about one out of five autopsies upon men over 50 years old, one or more small cysts, about the size of a lentil, usually of a hemispherical shape, sometimes polypoid or pedunculated, are found situated beneath the tunica vaginalis on the convex surface of the epididymis, or more rarely at the middle part of its tail. They are transparent, opalescent, amber colored, and when opened, a clear fluid containing no spermatozoa escapes. They are the structures above described as the upper and lower paradidymi.

Other, occasional, similar, small cysts occur upon the surface of the epididymis, but in distributions so remote from that of the vestigial structures as to make origin from them difficult to conceive. The two are frequently confused, but Monod and Arthaud, observing that the lining of these cysts conformed with that of the tubules of the epididymis, suppose them to arise from

those structures as the result of fibrous transformation of the epididymis and pericanalicular sclerosis of its tubules with intermittent obstruction followed by dilatation of the patulous portions of the interrupted tubules.

Other small cysts are supposed to arise through cystic dilatation of the vasa aberrantia, whose greater length and more superficial positions enable larger cysts to be formed.

From these small cysts without spermatozoa, which vary about the size of a pea, to the so-called large cysts that vary about the size of a walnut, one usually passes without intermediate stages. This suggests that attention is not attracted to the cysts until about the size of the walnut is attained, for all of the large cysts must have originally been small. But one notable difference is the presence of spermatozoa in most of these large cysts. This has made many suppose that they must originate otherwise than from the Wolffian vestiges, and perhaps some of them do. But it is well known that in the female sex the vestiges of the Müllerian and Wolffian structures are prone to undergo cystic dilatation, and therefore no matter for surprise that they should not do so occasionally in the male. When the general proneness of vestigial structures to undergo cystic dilatation is considered, and the correspondence in position between these cysts and the vestigial structures of the testis and epididymis considered, it seems only reasonable that the cysts should originate from the vestiges.

The larger cysts usually occur below the head of the epididymis, between it and the testis. Usually about the size of a walnut, they are occasionally as large as a hen's egg. The epididymis stretches over the cyst, and so to speak, becomes a part of it. The cysts are nearly always unilocular, and are filled with an opalescent fluid in which spermatozoa in varying quantities are usually found.

The presence of the spermatozoa was the stumbling block. It was argued that if the cysts developed from the embryonal vestiges there was no means by which spermatozoa could mingle with their contents, but if they were developed through the distension of seminiferous tubules or excretory passages, their presence was only natural. Or, if the cysts were formed through the dilatation of the vasa of Haller, the presence of spermatozoa could easily be accounted for through the free communications between those passages and the vas deferens. The theory of development from the vasa of Haller appealed strongly to Vautrin and Roth. But the argument is really of no force, because as was pointed out by Curling and Follin, supported later by Broca and Luschka, all of whom adhere to the Wolffian origin of the cysts, the spermatozoa easily find entrance into the cysts from adjacent seminiferous or excretory tubules, which being in close relationship to the cyst, are stretched and finally ruptured establishing a minute connection with it and the seminal passages for a time.

However, the matter is rather of academic than of practical importance as the cysts rarely grow large enough to require surgical intervention, and rarely cause enough pain or other adverse symptoms to disturb the patient.

Occasionally such a cyst is mistaken for a supernumerary testis. This ought only be possible when the cyst is too small to fluctuate, and is unusually firm. It is also sometimes mistaken for some form of hydrocele. The demon-

stration of spermatozoa in fluid aspirated from it ought at once make the diagnosis clear.

In Either Sex

In the course of its atrophy in the female, and its change from a urinary to a sexual organ in the male, followed by its transplantation from the upper part of the abdominal cavity to the scrotum, some of the tubules of the Wolffian body occasionally become separated and sequestered in the retro-peritoneal tissues. Subsequent atrophy probably disposes of them, but occasionally one may escape destruction and later give origin to an unexpected and difficultly explained lesion.

Such, at least is the assumption in regard to a few singular cystic growths of the retro-peritoneal tissues. One of these, reported by A. P. C. Ashhurst, was a cyst about the size of a fetal head, situated in the right side of the abdomen of a woman of 26 years of age. It extended from the inguinal fossa toward the umbilicus, and was behind the peritoneum which slid over it freely. It was filled with about a litre of fluid that is described as being "like spring water." Microscopic examination showed it to be lined with a single layer of columnar epithelium that rested upon a thin layer of fibrillar connective tissue, of which the wall of the cyst was formed.

Ashhurst believes this to be derived from such a Wolffian vestige, and bases the supposition upon a somewhat similar case reported by La Pointe. It also occurred in a woman about 34 years of age, was of about the same size, and was situated in the right flank, infringing upon the iliac fossa by its upper pole. It was unilocular, and when examined microscopically, after removal, was found to be lined with cuboidal epithelium, and to resemble the glomerules or canals of the Wolffian body as they appear in the parovarium.

PERSISTING VESTIGES OF THE WOLFFIAN DUCTS

In the Female

The Wolffian duct that should entirely disappear in the female, sometimes persists here and there in vestigial form, the most frequent situation being low down in the broad ligament at the level of the body of the uterus or upper part of the vagina. Such vestiges are known as Gärtner's ducts and from them cysts occasionally arise. It is not always possible to differentiate such cysts from those arising from the paroöpharon except in cases in which their lower position is clear.

PERSISTING VESTIGES OF THE PRONEPHROS

In the Female

The pronephros is an embryonal structure most of which is of very temporary duration in mammalian embryos. It is the homologue of a structure permanent and important in certain fishes (hag-fish), temporary, and important in bactrachians, but existing only during the embryonal period in birds and mammals, in whom it may be of no importance, and in whom it occurs only as a vestige of atavistic and phylogenetic significance. That it ever subserves any function in the embryos of man is a matter of doubt.

It arises from the mesoderm of the embryo when it is about 3 mm. in length, first appearing as two solid cords of cells that arise from the middle plate of the mesoderm, and extend from a point high up near the heart, to near the posterior end of the embryonic body. Soon they become hollowed out and form definite duct-like structures that end blindly above but open into the cloaca below. By this time they are known as the Wolffian ducts. Several short transverse tubular structures are found attached to the upper part of each, and are the true pronephric glands. If, as some embryologists think, these tubules are in connection with the ducts, the whole can be considered to correspond with a gland. But such connection is uncer-

tain. The only reason for mentioning these peculiar and uncertain structures is their occasional vestigial survival in both sexes. In the female these occur in the form of minute cysts, rarely larger than a pea, attached to the fimbriae of the Fallopian tube, where they are known as the hydatids of Morgagni. They rarely become large enough to be considered as of pathological interest.

In the Male

The homologue of this same structure is to be found in about 90% of male cadavers, where it is known as the *unstalked or sessile hydatid*. It has a length of about 5 to 10 mm., breadth of about 3 to 5 mm. and is attached to the upper pole of the testis, close to or slightly overlaid by the globus major of the epididymis. If its free end be carefully examined it is frequently found to show a shallow, funnel like depression surrounded by a dentate margin, the whole suggesting, as Piersol says, an oviduct in miniature. It rarely plays any part in pathological disturbance, though capable of cystic distention.

SOLID TUMORS ARISING FROM WOLFFIAN AND OTHER VESTIGES

In the Female

Adenoma and Carcinoma of the Ovary

Many of the vestigial structures examined have been found to give origin to both cystic and solid morbid growths and to both benign and malignant tumors and those of the sexual organs are no exception to the rule.

According to Kelly and Noble, about 15% of all ovarian tumors turn out to be carcinomas. Glockner asserts that no less than 46% of all ovarian carcinomas are bilateral, a matter that is difficult to understand. Some suppose that under these circumstances the disease is not primary in the ovary at all, but in some other organ, as the breast, for example, but there is no evidence of this in most cases. Kelly and Noble declare it bad practice to remove only the visibly diseased organ when carcinoma of the ovary is suspected, lest the disease later appear in the other organ.

Carcinomas of the ovary are solid in about 10% and cystic in the other 90% of the cases. As the two varieties have more or less individuality, it seems appropriate to describe them separately.

1. *Solid Carcinoma of the Ovary.*—These may be either scirrhus or encephaloid, and rarely attain to a greater size than the fist or a cocoanut, may be soft or firm, and may contain cystic spaces. In the experience of Kelly and Noble, the scirrhus carcinomas are always bilateral.

They form round, ovoid or kidney shaped tumors not infrequently appearing like enlarged ovaries. The diagnosis of the condition may not be possible until the lesion is examined with the microscope.

The isolated anatomical relations of the ovary, which Matthew Duncan first pointed out, afford exceptionally favorable opportunity for enucleation before a malignant disease has either invaded the surrounding tissues or distributed to other viscera. In many cases the removal of the ovary is sufficient to cure the disease. At least, it never recurs. In some cases there is local return; in less favorable ones infiltration of the adjacent organs, spread to the peritoneum, pleura, lungs, and in rare cases generalized distribution throughout the body may occur.

The microscopic structure of these tumors varies. In some cases they have all the usual characteristics of carcinoma so well developed that there is no question about the diagnosis; in others the tissue is so uniformly cellular, as to make one hesitate whether the tumor is not sarcoma, in spite of the large size of the cells and abundance of the cytoplasm.

2. *Cystic Carcinoma of the Ovary.*—This group seems to embrace three separate though closely related entities, first, carcinomas that are essentially cystic from the beginning; second, carcinomas that become cystic as the result of internal changes, and third, cystic tumors of originally benign nature that later show carcinomatous behavior.

These carcinomas may develop from Pflüger's tubes, the epithelium of the Gräffian follicles, the epithelial structures in dermoid cysts, or the epithelial structures in embryomas. It may not be possible to determine what the source of a particular tumor is, but that does not matter; the tumors are all carcinomas, behave as such, and should be treated as such and completely eradicated when possible.

In the Male

Adenoma and Carcinoma of the Testis

Pillier and Costes recognize two varieties of carcinoma of the testis, the *Wolffian carcinoma*, and the *seminiferous carcinoma* or *seminoma* of Chavessu.

1. *The Wolffian Carcinoma.*—This rarely attains to a size greater than a turkey's egg. It is soft, and filled with pea-sized cysts, containing mucus. Malassez called them "mucoid epitheliomas," and others have spoken of them as "cystic disease of the testis with malignant development."

The epithelial cells are distinctly columnar, arranged largely in pockets with well disposed cellular linings, the larger pockets forming the cysts.

Occasionally ciliated cells are found, and some of the linings of the cystic spaces have many goblet cells. Sometimes the new growth bears a striking histological resemblance to the epididymis. Its destructiveness lies rather in its disposition to replace the testicular tissue by its own newly formed tubular extensions, than by the cell infiltration and dissemination of ordinary carcinoma.

This form of carcinoma of the testis has been known to occur as early as the sixth month of age, and at all ages between childhood and old age; but its most frequent occurrence is between the 25th and the 45th years. Its first appearance is that of a general enlargement of the testis which, maintaining its normal form, slowly or rapidly increases until as large as a man's fist or even a cocoanut. The skin and deeper tissues of the scrotum usually remain free, and moveable, for a long time. But metastasis to the lumbar and retro-peritoneal lymph nodes may occur at any time. So long as the tumor is local it may be possible to remove the organ without return of the disease, but as soon as it spreads to the lymph nodes, it becomes inoperable.

2. *The Seminiferous Carcinoma or Seminoma.*—This tumor was supposed by Chavassu to arise from the seminal cells, and his view seems to be pretty generally adopted. "The epithelial cells, the dominating elements of the neoplasm, call attention to themselves because of their peculiar appearance. They are
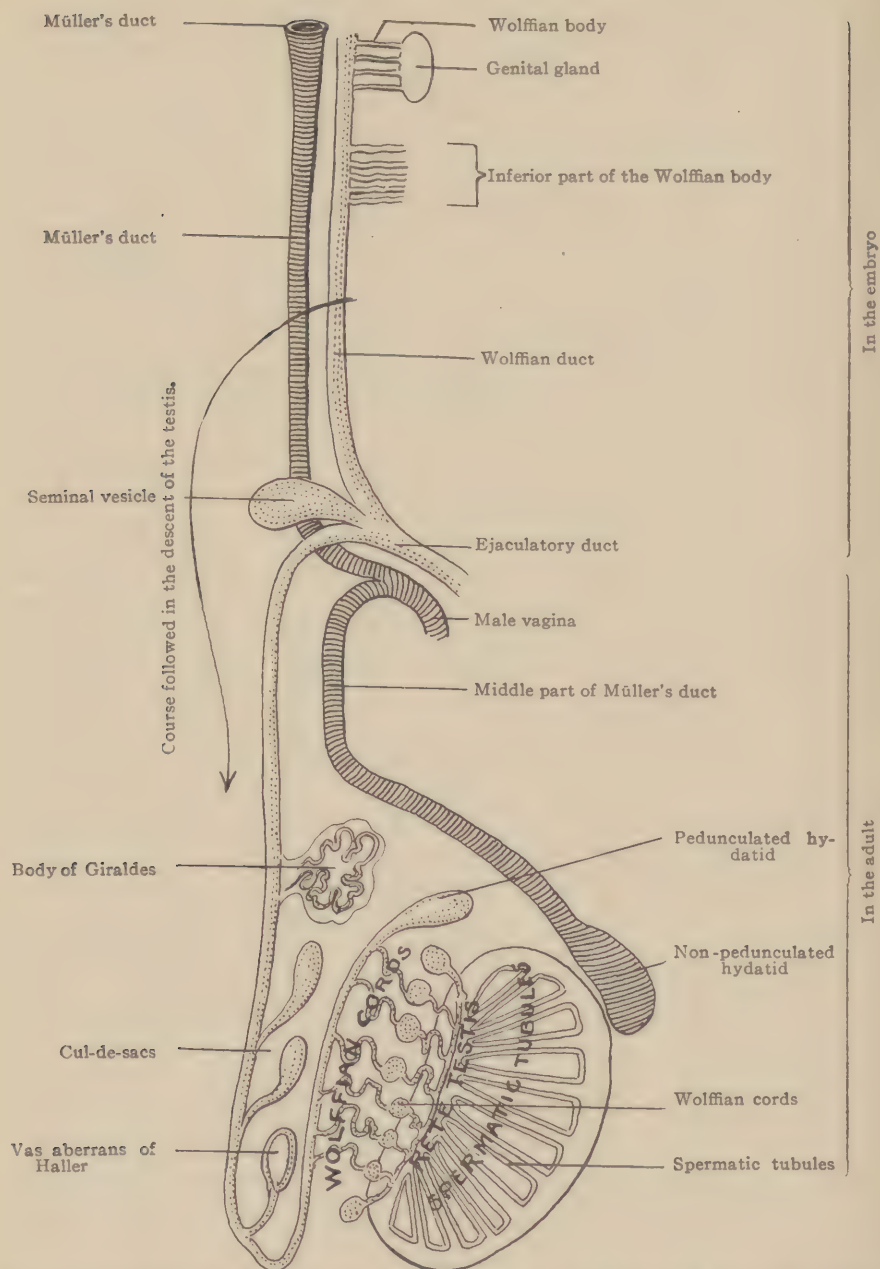
FIG. 115. —Diagram showing the formation of the testis, and the parts from which may develop the seminal and Wolffian epithelial tumors. (*Redrawn from Forgue.*)

very large, spherical cells with a regular contour, a large clear nucleus, and numerous nucleoli. They do not look like anything but the cellular elements of the Pflüger's tubes, according to Pillier and Costes, the male ovules remaining at their embryonal stage, and not forming spermatozoa. They are, then, not derived from the cells of the seminiferous tubules, but from the undifferentiated cells that ought have become the cells of those tubules."

"According to Curling, the testicular tumors start in the corpus of Highmore, which is the junction of the two parts composing the testis, the spermatic ampoules or tubes of Pflüger, and the Wolffian parts, the epididymis, efferent cones and body of Highmore, of which the canals come to connect with the male tubes of Pflüger, or seminiferous tubules."

"Let us suppose with Pillier, that this junction of the two elements did not progress normally, but that there remained seminiferous tubules in excess of the Wolffian tubules with which they were to connect. Then such elements, having nothing to do, might undergo atrophy and disappear, or they might, on the other hand, undergo proliferation, and then there might result either of two tumor formations, the one depending upon proliferation of the seminal ampoules would be a seminiferous carcinoma, or seminoma, the other, depending upon proliferation of the Wolffian ducts would be a Wolffian carcinoma."

The seminiferous carcinomas form considerable sized tumors whose cut surface is marbled by various tints of rose, gray or yellow. Microscopically the yellow color is found to depend upon the presence of pigment derived from hemoglobin in the necrotic areas of the tumor tissue.

Forgue says, "the morbid tissue can be reduced to a certain number of identical cellular groups: (1) An internal zone formed of the seminiferous tubule and its debris. (2) A zone of reticulated tissue, in which the lamellar sheath of the tubules has disappeared. (3) An eccentric border formed by the connective tissue of the framework of the gland.

According to the respective importance of the cellular elements and connective tissue framework, the tumors may be divided into:

1. *Encephaloid Carcinoma.*—Here abundant neoplasmic cells are grouped in islands in a matrix of connective tissue charged with branched or star-like cells which can be confounded with the reticulated tissue of lymphadenoma, if one does not notice that the cells are epithelial and not lymphatic, or with sarcoma, if the cells concentric to the epithelium proliferate in concentric masses.

2. *Scirrhus Carcinoma* —This as usual, is a hard tumor with dense connective tissue stroma, and epithelium in the form of narrow and elongate alveoli filled with heaped up polyhedral cells.

PERSISTING VESTIGES OF THE WOLFFIAN DUCT

In the Female

The ureters, upon which the metanephros will later develop on each side, make their appearance as buds from the lower part of the Wolffian ducts. A short time subsequently, as the bladder is formed, that part of each Wolffian duct lying between the uretral bud and the future bladder is drawn up and spread out in such manner as no longer to appear as a duct but as a flat-

tened surface which assists in the formation of the posterior wall of the bladder. In very rare cases this part of the developmental process miscarries and the lower part of the Wolffian ducts persists, bringing the ureters into relation with the vagina or vulva instead of with the bladder. Under these circumstances, the first symptom to attract attention is incontenence of urine. When a visual examination of the parts is made, two small orifices are discovered, one on each side, in the vestibule, in the vagina, or quite close to the meatus urinarius, from which urine constantly dribbles. A catheter introduced into either of them finds a long passage which ascends towards the kidney. The urethra is permeable, and through it the bladder can be entered, but it never contains urine. The difficulty lies in the fact that there is no connection between the ureters and the bladder, which makes the latter useless. When colored fluid is injected into the bladder, it does not escape from the abnormal passages.

Kirmisson has reported such a case. Though a very rare malformation, it is of surgical interest and importance because it can be corrected through the implantation of the ureters into the bladder, and the restoration of the normal relations.

A few cases are on record in which the ureters have normally emptied into the bladder, but that portion of the ducts above them, instead of disappearing by atrophy, has persisted, either as a blind cul-de-sac, or as a solid cord, or as a partly pervious structure. In a case of this kind reported by Boix, an elongated cystic mass was joined to the right vaginal wall along its inferior extremity. It measured a centimetre and a half in length, and projected into the vagina so as almost to close its lumen. There was a second cyst on the outside of the vagina, and the two were bound together by a kind of pedicle.

In a case reported by Ozerme, there was accidentally found, in the body of a woman 35 years of age, a fibrous cord 35 cm. long that connected the right kidney with the neck of the uterus. It was hollow in the middle though closed at the ends, and was accompanied by a normal ureter.

Such vestigial structures occasionally give origin to cysts, whose unusual position may be exceedingly perplexing if the possible occurrence of such vestiges is unknown.

PERSISTING VESTIGES OF THE NOTOCHORD
CHORDOMA

At the time that the ectoderm on the dorsal surface of the embryonic disc is showing the groove and ridges that later form the medullary canal, the subjacent endoderm is forming a band of cells that extends from the position of the future pharynx to the opposite end of the embryo body. It is the *notochord* or *chorda dorsalis*. At first flat, the band becomes convex anteriorly, and its sides close in more and more until it becomes a hollow tube. But it does not remain so, for its cells first enlarge and close the lumen, then undergo transformation into a solid elastic structure surrounded by a cuticle secreted by the cells themselves.

It is about this axial structure that the future spinal column develops, after which, its purpose having been accomplished, it disappears except for occasional vestiges that are sometimes found in the central parts of the inter-vertebral discs of infants, rarely persisting until later life, and small nodules that occur about the sphenoid bone and the coccyx.

No tissue of the adult human body resembles that of the notochord. It consists of a soft, homogeneous translucent matrix, in which are embedded

custers of large vacuolated cells. It more nearly resembles cartilage than any other tissue, and is frequently mistaken for it. But the vacuolation of the cells is characteristic. Virchow, however, mistook the tissue for cartilage, and described certain tumors of the spheno-occipital region, in all probability derived from notochordal vestiges as "ecchondroses spheno-occipitalis." W. Müller first recognized the true nature of the tissue, and Ribbert, who paid great attention to it, found notochordal vestiges present in about 2% of autopsies.

They usually appear in the form of single or multiple, soft and gelatinous rounded masses, usually situated in the clivus Blumenbachii, i.e., the slanting surface of the body of the sphenoid flone between the dorsum and the basi-
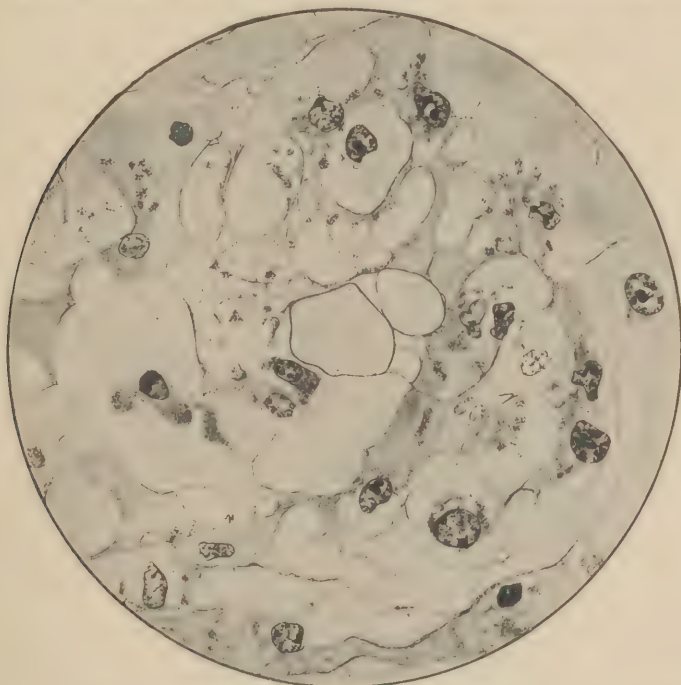
FIG. 116.—Chordoblastoma. Numerous vacuoles present, some with well defined walls. (*Mallory*, "*Principles of Pathologic Histology*.")

occipital. They are rarely larger than a pea or a cherry, are in the mid-line, where they pass through narrow openings in the dura and come into relation with the pia along the basilar artery on the basilar surface of the pons. They are so slightly attached to the tissues that they are usually left behind when the brain is removed. That fact together with their generally unobtrusive character probably explains why they are not more frequently observed and reported. Their small size and soft consistency prevents the occurrence of any symptoms from pressure.

Coccygeal cordomas have been reported by Feldmann, Vecchi, and Albert. A large chordoma of the cervical region was observed by Klebs, and another large tumor of the same region by Hassner.

Ewing points out that the diagnosis of chordoma is by no means always easily made, a fact that the author can corroborate, as he has several times

found small rounded bodies in the position in which they might be expected, but found them structureless upon microscopic examination. They seemed to consist of little masses of soft jelly surrounded by a capsule.

In such cases the cells have probably disappeared by atrophy, when, of course there is nothing left upon which to base the diagnosis.

Certain malignant tumors have been supposed to arise from notochordal vestiges, but there is always difficulty in proving such histogenesis.

The gelatinous nature of the tissue, and the vacuolation of the cells which are supposed to be characteristic, also connect it with gelatinous carcinoma, and Ewing thinks that the malignant chordoma reported by Feldmann, may have been a gelatinous carcinoma of the intestine invading the sacrum. At least, he has seen such tumors that exactly corresponded with what Feldmann described.

PERSISTING VESTIGES OF THE BLASTEMA OF THE METANEPHROS

Congentially Cystic Kidney

The metanephros, or permanent kidney, develops about the upper extremity of bud-like diverticula that are given off from the Wolffian ducts not far from their lower ends, and grow upwards and backwards, pushing their way behind the Wolffian bodies. About the upper caecal end of each a mass of mesenchyme collects, increasing as the tube lengthens and its blind end divides into a number of short branches, each of which becomes, a caecal pouch, or primary renal vesicle, or calyx of the future kidney. About each of these the contiguous mesenchyme develops so as to form a number of more or less separate lobules surrounded by a common capsule.

If the blastema itself be examined at this time, it will be found to contain numerous cellular condensations, solid at first, but soon hollowed into a tubular form, each assuming a sigmoid shape. One end of each of these S-shaped tubes is continuous with the neighboring primary vesicle and each is the beginning of a future uriniferous tubule. As more and more mesenchymal cells collect in the S-shaped curves of the blastema, they receive branches of the renal artery to form the future glomeruli, about which the blind ends of the tubules invaginate to form the capsules of Bowman. The upper curve of the S-shaped tubule eventually develops into the proximal convoluted tubule and the loop of Henle, the lower into the distal convoluted tubule and the arched collecting tubes. Thus the entire uriniferous tubule develops from the original blastema. It must, however, to be useful, connect with a glomerula at its upper end, and effect a communication with the developing ureter below. The kidney has originally about 18 lobules, which amalgamate as the formation of the pelvis becomes completed, though traces of their original separations may remain throughout the entire life of the individual—*congenitally lobulated kidney*.

The most important developmental defects for consideration in the present connection are those that result from failure of the tubes of the blastema to connect with a glomerule at the upper end, and with a connecting tube at the lower end.

1. *Failure to connect with a glomerule.* Under this circumstance further development of the tubule would probably be interrupted because of the lack of the essential vascular structure from which its water supply is derived. It would, therefore either undergo atrophy and disappear, or remain in an embryo-

nal form, appearing as a strand of cells. Single structures of this kind might easily escape observation, but where a number are closely approximated, they form peculiar and definite areas the nature of which is not always clear. Ewing figures these in his book upon the "Neoplastic Diseases," and believes that they may be the starting point of malignant tumors of the kidney. But what seems equally probable is, supposing that they have, at least in part retained their tubular structure, that they may collect fluid through exudation, and undergo cystic dilatation—a behavior consistent with that of vestigial tubules wherever they are to be found.

Fig. 117.—Congenital cystic kidney. (*Stengel and Fox, "Text-book of Pathology."*)

2. *Failure to connect with the collecting tube*. Under this circumstance, a continous or intermittent water supply is furnished by the glomerule, but having no means of escape, must be at once absorbed, or collect with distension and ultimate cyst formation.

In either case the defect may lead to the development of cysts in the kidney. These may be single, multiple or innumerable, according to the number of defective tubules. When their number is very small, it is impossible to definitely assign them to this cause, as they become confused with the simple retention cysts occurring in certain diseases of the kidney, notably chronic interstitial nephritis. But when they occur in great numbers and are of large size, congenital origin may always be suspected, and it is customary to call all such cases "*congenital cystic kidney.*"

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The congenitally cystic kidneys are quite commonly discovered at autopsy, in cases in which their occurrence has never been suspected, because they are usually unattended by any symptoms. It is certain that there are at least twice as many renal tubules as are needed to successfully carry on the function of excretion, else those from whom one kidney has been surgically removed must inevitably die. It may therefore be supposed, that as many as half of the renal tubules might suffer the congenital malformation under consideration, and lead to the formation of a vast number of cysts in each kidney, without seriously interfering with the health of the patient, until the damage done by the pressure of their increasing size, or the occurrence of some destructive disease interfered with the successful operation of the remainder.

FIG. 118.—Bilateral duplication of ureters and pelves. Duplication left kidney pelvis complete, with small hydronephrosis and stone of the lower pelvis. The two pelves of the right kidney united by common calyx. (*Braasch.*)

The congenitally cystic kidney is usually easily recognized. Both organs are about equally and uniformly affected, and are enlarged in proportion to the number and size of the cysts contained. The surfaces are covered with large or small transparent rounded eminences, sometimes flattened by the pressure of the capsule of the kidney which is frequently considerable thickened, sometimes projecting in hemispherical form when the capsule is unusually thin or the intracystic pressure great. They are of all sizes intermediate between visibility and walnuts, and are filled with clear watery fluid, yellowish or amber fluid easily recognizable as urine or modified urine, clear jelly, cloudy jelly, fluid or jelly with some crystalline deposit, or in more rare instances, calculi. They are, for the most part in the cortex, but may be anywhere.

IV. DEPENDING UPON THE ACCIDENTAL COALESCENCE OF PAIRED ORGANS DURING EMBRYONAL DEVELOPMENT

DOUBLE KIDNEY

Instead of a single diverticulum from each of the Wolffian ducts, and ascending to form the ureter, there seem in rare instances to be two, so that each kidney becomes provided with a *double ureter*. In more rare cases, the single diverticulum becomes divided so that the corresponding ureter is double for a part of its length. In still more rare cases there must have been a single diverticulum whose division gave origin to both ureters, as they both insert in the bladder at the same point, or there is a single ureter arising at the normal position, but dividing as it ascends, as in Braasch's case.

FIG. 119.

FIG. 120.

FIG. 119.--Double kidney. The higher position of the right and lower position of the left portions, as well as the manner in which the pelves turn anteriorly so that the ureters must cross over the kidney substance, are well shown. (*From a specimen in the Pathological Museum of the University of Pennsylvania.*)

FIG. 120.—Division of ureter at lower third. Left branch crosses spine and leads to a large hydronephrosis of the left kidney. Right kidney normal. Pyelograph obtained by using large catheter and inserting short distance into meatus. (*Braasch.*)

As the diverticula ascend to form the ureters, and become surrounded by the mesenchymal cap that is to form the parenchyma of the kidneys, they sometimes deviate from the normal path, and instead of diverging to opposite sides

of the spinal column, ascend on the same side. Under these circumstances, the organ normal to that side, always occupies the higher position, that deviated from the other side, the lower. The deviation is usually from left to right, and usually the right kidney is the larger, and the left may be found at any altitude from near the normal to the brim of the pelvis, or may prolapse into the cavity of the pelvis. The deviated kidney also commonly fails to assume its normal position with respect to its axes, its long diameter commonly being more transverse than normal. It may, indeed occupy a horizontal position.

If the organs ascending together come into contact at an early period, the developing substance of the one frequently becomes more or less blended with that of the other, so that *double kidney* results. The appearance of doubled organs varies, but the upper part with its ureter always corresponds with the organ normally belonging to the side upon which the deformity occurs, and the lower part with its ureter, to its fellow. There are always two pelves and two ureters. The ureter of the upper segment passes down to its own side of the bladder, that of the lower, crosses over to the opposite side.

Horse-shoe Kidney

If the rudiments of the kidneys, ascending in the normal directions to their future positions touch one another, partial coalescence of their substance may occur, later appearing as commissures by which the organs are connected. These vary considerably in magnitude. They may embrace the capsular substance only, so that the connection is no more than a slender fibrous cord, or they may appear as bridges of parenchymatous tissue passing between the organs binding them together more or less closely. In most cases the bond is broad and thick, and it may not be possible to say where the one organ begins and the other ends, but the line of separation is usually marked by a groove.

The isthmus consists of renal parenchyma with its full quota of tubules and glomerules, and frequently is provided with its own artery, arising from the aorta to supply it. The capsules of the organs continue over it.

The isthmus very rarely takes the form of a median bar, occasionally connects the upper poles of the conjoined organs, but in the majority of cases passes between the lower poles, and occurs in so massive a form as to transform the kidneys into a single organ of a U-shape, the "*horse-shoe kidney*."

Thus conjoined, the kidneys become heavier than normal, and so do not usually reach their normal altitude, but come to rest lower down, or subsequently sink, so that they are not infrequently found as low as the brim of the pelvis, where they overlie the promontory of the sacrum, or even its hollow. The right half usually is a little higher than the left.

The isthmus passed behind the aorta in cases studied by Nixon, Carlier, Kelly and Zeit, in front of it in all other reported cases. The renal vessels, both arterial and venous are nearly always anomalous.

Especial interest attaches to the ureters and pelves. As there is no disturbance at the time that the diverticula arise from the Wolffian ducts, there are

always two ureters, but one or both of them may be divided, so that the total number of ureters may be either two, three, or four. The position of the pelvis is altered as is shown in the following quotation from Rokitansky:

"The more complete the fusion, the lower is the position of the kidneys. The completely fused mass is commonly situated at the promontory or even at
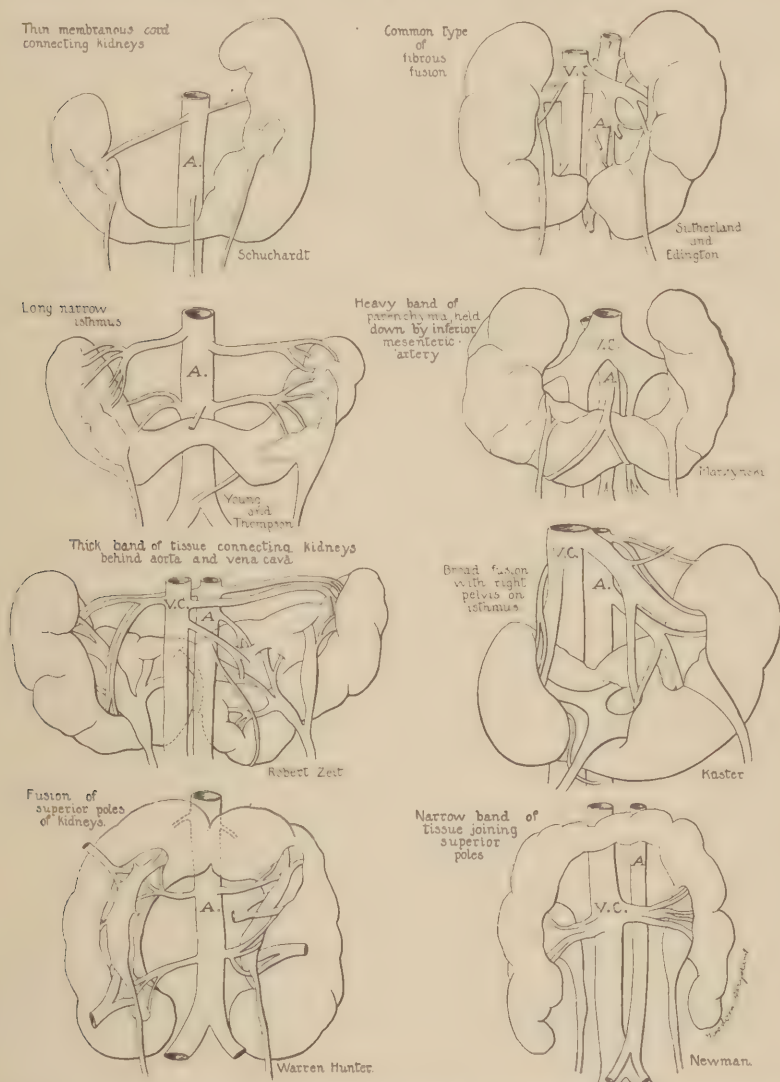
FIG. 121.—Horseshoe kidneys, showing variations in structure of isthmus. (*Judd, Braasch & Scholl.*)

the concavity of the sacrum. In the usual type of horse-shoe kidney, the renal masses tend to converge downward and inward, responding to the traction exerted by the commissure on the inferior poles. This is accentuated by the lordosity of the lumbar spine; and not infrequently the superior poles are found

widely separated. There is also a second abnormal deviation of position; the fusion prevents the complete rotation of the kidney on its vertical axis, leaving the pelvis facing anteriorly. The posterior surface of these kidneys is generally smooth, quite in contrast with the curiously retained markings of the fetal lobulations on the anterior surface."

When the isthmus is at the superior poles, the pelves are not affected by it, but when as is most frequent, it connects the lower poles, they frequently lie upon it, and the ureters must cross it. The pelves are frequently more or less divided and complex. The descending ureters, must sometimes bend upward, to a certain extent, in order to cross the isthmus, and are sometimes so angulated as to suffer partial obstruction. The relation of the pelves and ureters to the renal arteries and veins is usually very anomalous, and rarely twice alike.

The pressure of the isthmus upon the great veins and, indeed, upon the aorta itself is not without importance. In some cases the patient suffered from edema of the lower extremities, several cases are known to have had hyper trophy of the left ventricle of the heart, supposedly from the aortic obstruction, and another case is known to have had iliac thrombosis without other explanation than the venous obstruction..

Of 262 collected cases studied by Beyer, 18 only showed the isthmus at the upper poles. Of 16 cases observed at operation in the Mayo Clinic, and reported by Judd, Braasch and Scholl, 7 were hydronephrotic. They think the horse-shoe kidney to be predisposed to such diseased conditions as result from dilatation of the renal pelvis from obstruction of its outlet.

There is no certain way of diagnosing the condition during life, and it usually turns up unexpectedly at surgical operation or at autopsy.

V. DEPENDING UPON CONDITIONS EXTRINSIC TO THE EMBRYO, AND FOR THE MOST PART NOT HEREDITARY

I. IN LARGE PART DEPENDING UPON ADHESION, COMPRESSION OR CONSTRICTION BY AMNIOTIC BANDS

Encephalocele

Encephalocele may be defined as the congenital extra-cranial and extra-dural occurrence of a portion of the membranes of the brain, of the brain substance, or of both. It is also sometimes defined as a hernia of the cerebral substance through a cranial fissure.

It is always congenital, and usually apparent at birth, though there may be cases in which the position of the defect is such as to prevent it from being immediately seen, as, for example, the rare cases in which the mass projects anteriorly into the nasal fossa or pharynx.

But ordinarily the malformation is immediately recognized, the child being born with a larger or smaller saccular tumor, of fluctuating or doughy quality

attached to some part of its cranium by a constricted area like a broad pedicle. The common position is posterior, in the occipital region; a few are anterior and show upon the face; a very few are lateral.

Houel, who collected 93 cases, found 68 to have been in the occipital region, 16 in the fronto-nasal region, and only 9 to have been lateral.

FIG. 122.—Meningocele. In this case the brain substance all remains within the cranium, and only the pia-arachnoid projects to form a sac filled with fluid. It is the most simple lesion, and the one that offers the best hope of successful operative treatment. (*Redrawn from Okinczyc.*)

They vary greatly in size, some being quite small, others as large as the head itself. Those occurring posteriorly and laterally, are covered by the hairy scalp, those upon the face by the integument.

The consistency varies according to the contents, and it is customary to divide them into:

1. *Meningoceles.*—In these only the membranes of the brain appear extracranially. The tumors fluctuate more or less, are translucent, become tense during forced expiration, are more or less reducible, and occasionally pulsate.

2. *Encephaloceles.*—In these, in addition to the membranes, there is a larger or smaller mass of brain substance outside of the cranial cavity, giving them a somewhat doughy quality, preventing fluctuation, and making them opaque. They are usually attached by a broader base, pulsate distinctly, become tense upon forced inspiration, cannot be reduced, and produce symptoms of compression of the brain when efforts to reduce them are made.

3. *Encephalo-cystoceles.*—These are usually larger, contain greater quantities of brain substance in which there is a space commonly in communication with the ventricular cavity of the brain. They may be somewhat lobulated, may fluctuate more or less distinctly, are in part translucent, may pulsate, become firmer upon forced expiration, cannot be reduced, and occasion symptoms of compression of the brain when attempts to reduce them are made. They may be attached by a broad base, or be distinctly pedunculated, and they are apt to be accompanied by palsy and deformity elsewhere.

Whatever its variety, the sac always communicates with the cranial cavity through an opening in the bony tissues and the dura.

In the case of the posterior lesions the opening may correspond fairly well with the inion, in the case of the higher lesions, with the bregma, and in the case
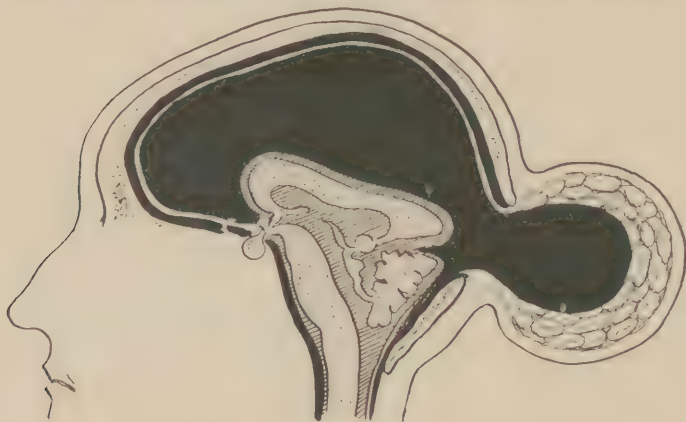
FIG. 123.—Encephalocele or encephalomeningocele. The frontal region is depressed—"tête de chat," and the brain substance projects (encephalocele) through an opening in the occipital region, surrounded by the pia-arachnoid that forms a sac filled with fluid (meningocele) and is covered with the scalp, there being no dura. (*Redrawn from Okinczyc.*)
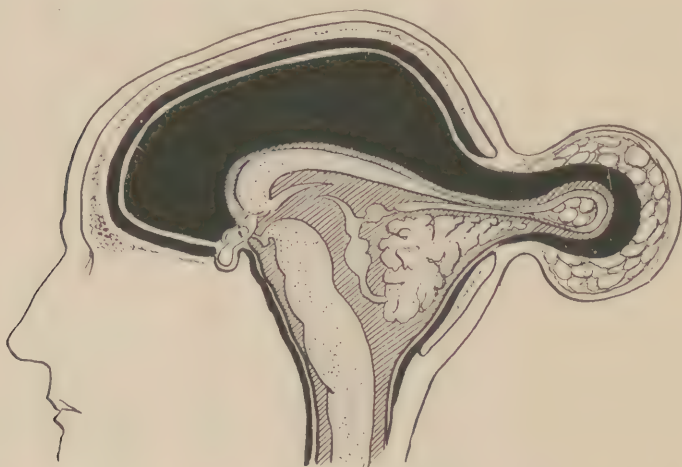
FIG. 124.—Encephalocystocele or hydroencephalocele. In this variety the ectopic brain tissue contains a cavity filled with cerebrospinal fluid, and communicates with the general ventricular cavity. (*Redrawn from Okinczyc.*)

of the rare anterior lesions with the gabella, but the correspondence is inexact, and sometimes the protrusion takes place laterally in the temporo-parietal regions. The occipital lesions are sometimes associated with a fissure of the occipital bone that continues into a cervical rachischisis. The frontal lesions nearly always appear upon the face usually at the inner angle of the orbit,

rarely at its external angle, and communicate with the cranial cavity by means of an opening situated somewhere about the body of the sphenoid bone. If they project into the pharynx, as happens in very rare cases, the bony opening is found to pass through the cribriform plate of the ethmoid bone.

The anterior lesions are almost exclusively encephaloceles.

When one of these lesions is carefully examined, some part of the surface will not infrequently be found to exhibit a kind of scar, and in some cases much of the covering will be made up of a peculiarly wrinkled and scarred integument, to which fragments of the fetal membranes may be attached. This, which can only be found upon the externally situated lesions, and never in those in the pharynx, is supposed to give the clue to their origin, and to it return will be made later. Upon the removal of the scalp or other superficial covering, the pia-arachnoid is exposed: *there is no dura.* This is of great importance, and to it return will be made later. If the lesion be a simple meningocele, the membranes form a sac filled with cerebro-spinal fluid; if it be an encephalocele, they cover a larger or smaller mass of brain substance. This may be as large as that which remains within the cranium, and in some cases is

FIG. 125.—Anterior encephalomeningocele, projecting at the root of the nose. (*Redrawn from Kirmisson.*)

found to have recognizable anatomical configuration and comprise a cerebral hemisphere or a lobe of the cerebellum that seems to have escaped from its normal environment, giving the impression that the condition is one of hernia cerebri. But in other cases it will be found that the parts outside of the cranium duplicate those on the inside, and in still others that they are in no way related to them.

It seems proper to deduce from this that the dislocation of the structure occurred at an early period of embryonal life, and before the cerebral substance had completely differentiated into its normal parts, some of which later developed normally, others abnormally and in some cases with an excessive formation of cerebral tissue.

If the lesion be an encephalo-cystocele, a cavity communicating with the general ventricular cavity of the brain will be found.

The malformations are extremely dangerous and commonly fatal. When they are very large, it may be difficult for the children to be born. The increase in the size of the head, and the posterior position of the enlargement, usually cause posterior retraction and determine that the face present at the pelvic outlet. Subsequent pressure, either by the accoucher in attempting to adjust the position, or by the uterine contractions not infrequently cause the unprotected tissues to rupture, and the cerebro-spinal fluid and brain substance to escape.

If the child be born alive there is always imminent danger that the delicate nervous tissue in the sac, undefended by a bony encasement, will be traumatically injured, as well as equal danger that the growth of the lesion from increase of its cerebro-spinal fluid, will cause the coverings to become so thinned as to rupture, with escape of cerebro-spinal fluid, infection and death.

FIG. 126.—Enormous occipital meningocele.

Encephaloceles do not seem to have attracted attention very early, perhaps because of their rarity, perhaps because they were confused with other lesions. Louis, for example, supposed them to be perforating tumors of the cranium. Geoffry Saint-Hillaire seems to have been the first to look upon them as embryonal malformations, and called attention to the wrinkled and cicatricial scalp with which they are covered, as of significance in explaining their etiology. He supposed that at an early period of embryonal development, the amnion became attached to the ectodermal covering of the primitive encephalon, drew it out of shape, and thus occasioned the deformity of the brain which later was followed by deformity of the developing skull. According to his theory the subsequent development is almost identical with that of the dermoids of the scalp already described. The interposition of the displaced tissue interferes with the perfection of the bones of the cranium which, per force, surround, but do not cover it, and thus leave a defect through which the brain tissue, or the membranes seem to project. In the case of the more rare anterior encephaloceles, the projection of brain substance having occurred before the face was formed, the features developed about it as best they could. For this particular class of lesions Okincyzc has a slightly different theory, supposing that they are arrests of development, for which a voluminous rhinencephaly failing to undergo the usual transformation into the olfactory bulbs is responsible. Spring, in 1854, considered encephaloceles to be cerebral hernias. He still has a few followers.

Ribbert declares that there is no single origin for the lesions, and offers four theories as appropriate:

1. They are inherited anomalies of development. This finds support in the observation of Davies, who delivered a child with an occipital encephalocele that was ruptured during labor, and was the second born of the same mother. The previous one had had anterior encephalocele with spina bifida.
2. They are the result of fetal hydrocephalus. It is difficult to understand how the pressure of hydrocephalus, which usually effects uniform enlargement of the fetal head, could bring about a local disturbance with escape of brain substance, and especially how it could do so without the mass being covered by the dura.
3. They are the result of adhesions between the cephalic vesicle and the amnion at an early period of development. This theory of Geoffry Saint-Hillaire seems to be most valid.
4. They are the result of intra-uterine pressure, as from diminished amniotic space by which the head may be compressed or retroverted so as to prevent the closure of the cranial bones. It is true that there is usually defective development of the cranium, but that is partly due to the fact that the cranial contents are diminished. The greatest malformation occurs in cases of very large encephaloceles, and is characterized by a very receding fore-head. The French writers call the deformity "*crâne de chat*,"

1. Okincyzc reminds us that.
   (*a*) The appearance of the cephalic portion of the central nervous system precedes the development of the cranium that is to inclose it, and
   (*b*) The cranium develops normally about a normal encephalon.

The importance of any malformation augments with the precocity of its development. Any accident to the early development of the encephalon may therefore interfere with the development of the cranium, and the nature of that accident, the character of the cranial imperfection. Thus, acephalia is accompanied by acrania; anencephalia by partial acrania, and ectopia cerebri by openings in the cranial wall.

Some of these malformations are remediable. The meningocele, the most simple, though frequently the largest, are probably most so, the encephaloceles, less so. Encephalocystoceles, at least when large are hopeless, and the infants so deformed usually die early.

The surgical difficulties to be overcome vary in different cases, but the general principle that the presence of brain substance in the tumor does not contraindicate operation should be kept in mind. The immediate prognosis is always grave because of the danger of infection and loss of cerebro-spinal fluid. The final success of operation apart from saving life is problematical, and must depend upon what nervous tissues are sacrificed in the excised mass, and the probability of palsy and mental deficiency being the result.

INTRA-UTERINE AMPUTATIONS

The umbilical cord is sometimes excessively long, and under such circumstances may become wrapped about the arm, leg or body of the fetus, where it leaves a distinct groove to mark its former position, and sometimes what is far more important, more or less atrophy of the constricted member. From such, it is an easy step, to pass in imagination, to those more rare and mutilated cases in which the child is born without an arm or leg, and account for the defect upon the supposition that the missing member has been amputated in utero, by an exaggera-

tion of the same constricting agency. But when the matter is carefully considered, and the soft and yielding nature of the substance of the cord taken into account, this seems to be a hasty conclusion; the probability that the cord itself would suffer destruction seems to be as great as that it could effect the amputation. But more important, and leaving one in greater perplexity, is the absence of the amputated part. What has become of the arm or leg that has been amputated? There are cases in which it is clear that amniotic bands have effected the partial and even complete amputations, but in such cases, the members are always there to give an account of themselves; in cases of supposed amputation by the umbilical cord, they never are.

The probable truth of the matter is that the parts are absent because they never were there; instead of being absent because they were amputated, they are missing because they never were formed. Such cases exemplify *ectromelia*, and are really *aplasia* or *agenesia* in which the parts supposed to be amputated have never been formed. There is in all probability no such thing as intra-uterine amputation effected by the umbilical cord.

II. DEPENDING UPON CROWDING OR MAL-POSITION OF THE FETUS IN UTERO, PRESUMABLY FROM DEFICIENCY OF AMNIOTIC FLUID

Under this heading will be considered a somewhat miscellaneous group of malformations, mostly affecting the extremities of the body, and of a character making it quite certain that they began at a comparatively late period of ante-natal life. Various theories of origin are given in explanation of each, and it is not so much because of any certainty that they are brought about in the manner indicated as because there seems to no more logical position for them in the classification adopted, that they find consideration here.

It is easy to conceive that in oligohydramnios, or deficiency of amniotic fluid, the fetus, having been subjected to crowding, compression, and unnatural flexion, may show the effects in some permanent malposition or atrophy.

Congenital Luxation of the Hips

Luxation of one or both hips is a frequent congenital malformation, forming, according to Albee, about 2% of all orthopedic conditions.

Between the years 1884 and 1894 Lorenz collected 253 cases, of which 30 were in males, 233 in females—88.8%. Seventy-seven were bilateral, 100 were left sided, 76 right sided.

The condition is sometimes apparent at birth, sometimes not until the child is ready to walk. This is partly because it is most noticeable when the child is in the upright position upon the feet, and when he walks.

These characteristic signs then show themselves:

1. *Lordosis.*—This is a forward curvature of the spinal column that is most marked in the lumbar region, and makes the back hollow and the belly protuberant. It is much more marked in bilateral than in unilateral cases.
2. *Waddling Gait.*—This is peculiar, and is also known as the "duck-like waddle," the sailor's gait, etc. It is also much more marked and better developed in the bilateral cases, and may be described as follows: The body is lurched toward the side upon which the weight is supported, as the limb of the opposite side is lifted up and thrown forward, then inclined toward the other side, and the other limb thrown forward. It is the result of the combination of various factors: the lordosis, the shortening of the fomora, the functional disability of the gluteal muscles, the displacement of the heads

of the femora, and probably also of an abnormal degree of mobility of the lumbar region of the vertebral column.

3. *Deformity.*—This differs according to the nature of the case:

(a) *Unilateral Cases.*

In these the distance between the anterior superior spinous process of the ilium and the internal malleolus of the affected side is shortened, and the great trochan-

FIG. 127.—Unilateral dislocation of hip, back view. (*Young.*)
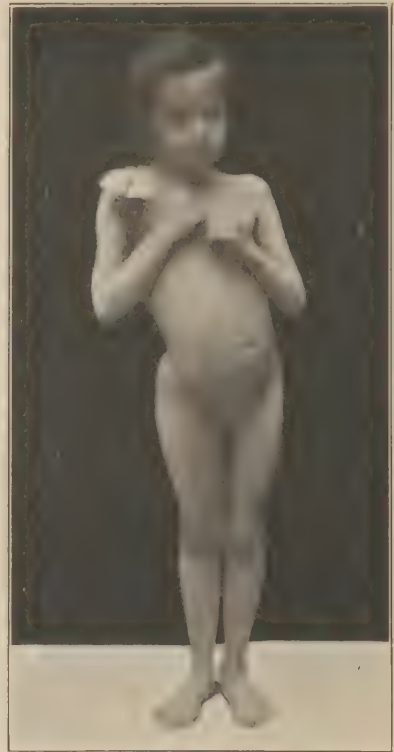
FIG. 128.—Same, front view. (*Young.*)

ter is always found above a line drawn from the anterior superior spinous process of the ilium to the most prominent part of the tuberosity of the ischium—Nelaton's line.

(b) *Bilateral Cases.*

In these the limbs seem to be too short for the body, and the thighs too short, in proportion to the length of the lower legs. The great trochanters are abnormally prominent and the upper parts of the thighs seem to be abnormally far apart, so that the perineal space is increased in breadth, while the buttocks are flattened, and the tuberosities of the ischiae are not covered by the gluteus maximus muscles.

The explanation of these peculiarities, and especially of the deformities is made clear by an examination of the hip-joints, which show deformity of the acetabular cavities, of the heads and necks of the femora, of the pelvis and of the soft parts. Since the common and practical use of the X-rays, it has become possible to determine the precise nature of the deformity in every case, and from such examinations, the following are seen most frequent:

"The acetabulum shows defective development of the rim, especially at the upper and posterior parts; thickening and elevation of the floor, and gradual transformation into a triangular depression with its apex in front and below, and its base above and behind. The head of the femur is atrophic and conical, its neck short, depressed, and anteverted. In some cases the head may even be absent; in others the neck may be twisted. Not infrequently the head of the femur becomes flattened through striking upon the the ilium.

FIG. 129.—Bilateral dislocation of hip, front view. (*Hopkins.*)   FIG. 130.—Same, side view. (*Hopkins.*)

The pelvis varies according to the unilateral or bilateral character of the case. In the latter it is tilted forward at an angle of 90 degrees.

The lumbar lordosis affects the position of the sacrum which is tilted outward, and greatly curved. The innominate bones which are small, occupy a more vertical position than normal, the iliac crests being approximated, and the tuberosities of the ischiae turned outward. The capsular ligaments become stretched as the greater part of the weight of the body falls upon them. On each side the ilio-psoas tendon crosses the capsular ligament, and the round ligament passes through the point of constriction, sometimes giving an hour-glass shape. All of the muscles that arise at the pelvis to insert in the thigh are apt to be shortened. The actual position of the dislocation is usually upward and backward."

These anatomical conditions have lead many to suppose that the cause of the deformity is purely mechanical. But there are various other theories, which Kirmisson divides thus:

1. Theories founded upon the existence of pathological condition of the joints.
   (a) That the luxation depends upon traumatism during intra-uterine life, or at the time of birth.

(b) That it depends upon primary disease of the articulation—elongation of the ligaments.

(c) That it depends upon primary disease of the nervous system.

2. Theories regarding the condition as an arrest of development—dysarthrosis ilio-femoris congenita.

It is conceivable that a normally developed fetus might suffer later deformity, of such character as has been described, through malposition in utero, associated with oligohydramnios. If its limbs were strongly flexed upon its body and adducted, the effect would probably correspond to the requirements of the case. But it is difficult to be content with such an explanation in the face of certain other facts, one of the most important of which is the distinct heritability of the malformation. Ballantyne found a history of inheritance in 25% of the cases he studied. This might be explained by assuming that oligohydramnios also runs in families. But then comes that other matter of sex incidence. Eighty-eight per cent of the cases are girls. Why should females be more subject to the diastrous effects of the pressure and malposition than boys? It makes the condition rather appear as a defect of the germ-plasm linked to the female sex, than as an accident of intra-uterine life.

Other Congenital Luxations

Other congenital luxations, of the elbow, shoulder, knee and wrist occur, but require no additional consideration. Most of them seem to be referable to accidental injuries sustained by the fetus during birth.

CLUB FOOT

Club foot, Talipes, *pied bot*, or Klumpfuss, is another congenital malformation about the origin of which there are many theories and no certainties. The condition is common: Chaussier found it occurring 37 times in 23,923 births, or 1:636; Lannelongue 8 times in 15,229 births, or 1:1903; Bessel-Hagen 8 times in 1:1100 or 1:1200.

It may be congenital or acquired. When the cases are analyzed, they are found to include

1. Those occurring at birth without accompanying or antecedent demonstrable disease of the central or peripheral nervous system by which they can be explained.

2. Those present at birth in association with spina bifida or some other disturbance of the central nervous system to which they may be referred.

3. Those making their appearance during the early years of life as the result of disease of the peripheral nervous system.

4. Those making their appearance during the early years of life as the result of disease of the central nervous system.

The attempt has frequently been made to bring all of these cases together, and ascribe them to a common cause through some such argument as this: The cases that are acquired after birth, usually depend upon infantile palsy; many of the congenital cases are associated with spina bifida or some other condition that explains them, therefore the congenital cases probably depend upon some similar causes long antedating birth, no traces of which any longer show. But

in the great majority of cases there is no evidence whatever to indicate the past occurrence of any disturbance of the central nervous system, so the reasoning seems to be fallacious. The majority of children born with club feet seem to be normal in every other way.

But, if the condition is not to be explained as the result of disturbance of the nervous system, how is it to be accounted for?

Ferdinand Martin seems to have been the first to whom it occurred that club foot might be the result of prolonged mal-position of the fetus in utero, and the idea was quickly seized upon and popularized by Cruveilhier. The mal-position is supposed to result from deficiency of amniotic fluid, but in a few cases at least, as shown by Bessel-Hagen, can be referred to twisting of the umbilical cord about the feet. Kirmisson also observed a case in which this seemed to be the probable cause.

Eschericht regarded the deformity as depending upon arrested development by which the feet of the fetus maintained the position normal to early intra-uterine life. Berg, Kocher and others were favorably impressed by this view that was bitterly attacked by Scudder.

The former examined the feet of many embryos and feti, and found that in embryos of 30 mm. the feet are in complete extension; in those of 40 mm. are slightly turned toward the planter surfaces; in those of 90 to 100 mm. the feet are at right angles to the legs, and it is only during the late months of gestation that the feet ever show supination as the result of lack of space and intra-uterine compression as the quantity of amniotic fluid becomes diminished. Scudder examined 69 well preserved embryos and decided that it was only during the sixth week that the position and form of the inferior extremities were such as to make them subject to external forces. Thus, though some light has been thrown upon the matter, the evidence is not sufficient to overthrow the theory of Eschericht, or to suggest a new one.

Albee, in his "Orthopedic and Reconstructive Surgery" gives ten varieties of club foot, of which six are simple, and four complicated. They are as follows:

(a) Simple Forms.
    1. Talipes equinus (plantar flexion).
    2. Talipes calcaneus (dorsiflexion).
        In both of these the articulating center is the ankle joint.
    3. Talipes varus (adduction and inversion—supinated foot).
    4. Talipes valgus (abduction and eversion).
        In both of these the articulating centers are the ankle and medio-tarsal joints.
    5. Pes cavus. Increased convexity of the longitudinal arch.
    6. Pes planus. Flattened longitudinal arch.

(b) Complex Forms.
    7. Talipes equinovarus. Extension and inversion.
    8. Talipes calcaneovalgus. Flexion and eversion.
    9. Talipes equinovalgus. Extension and eversion.
    10. Talipes calcaneovarus with cavus. Flexion and inversion.

The varying frequency of the more common varieties is shown in the following tabulation of 1180 cases, though the varying nomenclature employed by the

FIG. 131.—Talipes equinus. (*Young.*)

FIG. 132.—Talipes calcaneus. (*Young.*)

FIG. 133.—Talipes equino-valgus. (*Young.*)

FIG. 134.—Talipes calcaneo-varus. (*Young.*)

FIG. 135.—Talipes calcaneo-valgus (*Young.*)

FIG. 136.—Talipes cavus. (*Young.*)

FIG. 137.—Talipes planus. (*Young*)

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different reporters made it impossible to bring their collections into complete harmony:

Reporter..........................	Tamplin	Ketch	Kirmisson	
Talipes varus.....................	703	14	4	721
Talipes equinovarus...............	...	151	140	291
Talipes equinovalgus..............	...	3	...	3
Talipes valgus....................	42	2	...	44
Talipes equinus...................	...	4	1	5
Talipes calcaneus.................	...	...	16	16
				————
				1180

According to the nomenclature adopted in the United States, the most frequent varieties of club foot are Talipes equinovarus and Talipes calcaneovalgus. Others are very rare in comparison.

I. *Talipes Equinovarus.*—This is by far the most frequent form of the deformity, and according to Williams, forms 77% of all cases. It is characterized by forced adduction of the foot upon the leg so that the sole is turned toward the median line, in association with internal rotation of the foot about its medio-tarsal articulation. According to Kirmisson, there are three degrees of this deformity:

1. The foot forms an obtuse angle with the axis of the leg.
2. It forms a right angle with the axis of the leg.
3. It forms an acute angle with it.

The pathological anatomy is exceedingly complex, nearly all of the tarsal bones participating, and undergoing modifications in shape.

II. *Talipes Calcaneovalgus.*—In this second most frequent variety, the foot deviates externally and is forcibly flexed upon the leg. The prominences of the tendo Achilles and of the calcaneum are effaced, and the heel is smooth. The relaxation of the tibio-tarsal articulation is sometimes so great that the dorsal surface of the foot is in contact with the anterior surface of the leg. The sole of the foot is flat, and upon its internal surface, the head of the astragalus and the tubercles of the scaphoid show as prominences.

The deformity of the tarsal bones, to which reference has been made seems to be sufficient evidence that the condition is of considerable duration at the time of birth. The club foot of the new born is not new; if it were so it would be easy to correct, but it is already old, and the tarsal bones deformed so that it is difficult to adapt them to new positions. And not only have the bones themselves thus become changed, but also their tendons, ligaments and attached muscles.

CLUB HAND

This is an extremely rare malformation, usually referable to congenital absence of, or congenital defective development of the radius or ulna, by which the malposition of the hand is readily explained.

In a few cases, however, both of the bones of the fore-arm have appeared normal, yet the hand mal-placed and deformed so that the condition is analogous to club-foot.

SCOLIOSIS

Scoliosis is excessive lateral curve of the spinal column, associated with more or less rotation. It is both congenital and acquired, but usually the latter.

It is very rare for the new-born infant to have a crooked spine, and young children rarely show it. Indeed, most of the cases seem to develop about the time of adolescence, and more than half of them are females.

The congenital cases, which alone interest us here, are usually easy to account for, and by careful examinations made with the X-rays, are found to depend upon deficient and supernumerary vertebrae and half vertebrae, unilateral cervical ribs, unilateral sacralization of the fifth lumbar vertebra, and a few other abnormalities by which the normal balance of the vertebral column is disturbed.

But there are a few cases in which all of these are absent, so that no cause for the curves can be discovered. Some refer them to ante-natal disease, others include them among the disorders resulting from mal-position in utero, with increased intra-uterine pressure perhaps resulting from deficiency of liquor amnii. But no adequate evidence of the occurrence of either of these factors has been produced, and the whole matter is one of surmise.

However, crowding of the fetus in utero can act as supposed. There was, some years ago, in the museum of the Woman's Medical College of Pennsylvania, a small deformed fetus, probably of about the fifth month, whose body was compressed into an ovoid form about the size of a goose egg. But what was most interesting in the present connection was the spinal column which showed a cork-screw-like twist through a half circle, with the result that the face and shoulders were directed posteriorly, and the trunk shortened so that the ribs were crowded against the pelvis. When the malposition was corrected, the tissues were found to have so completely accommodated themselves to the new relations, that they returned with a snap. It represented the extreme degree of scoliosis.

Acquired scoliosis may be but a congenital condition with retarded manifestation, for it is not uncommon for a number of cases to occur in the same family to indicate that heredity plays an important role in the etiology.

Naturally, any hereditary predisposition may be brought out through a variety of later acting factors such as habitual bad posture at school or at work.

TORTICOLLIS, OR WRY-NECK

This is an occasionally hereditary, usually congenital, sometimes acquired malformation, characterized by abnormality of the muscles of the neck, by which the head is drawn toward one shoulder, and the face made to deviate from the mid-line in the opposite direction.

It is rare, and, as so often happens, it is impossible to assign all of the cases, even when apparently much alike, to the same category.

A favorite theory assigns the condition to accidents occurring at birth, and in cases of difficult labor when instruments are used, and the head pulled upon and twisted, and it is not difficult to see that the explanation might be adequate.

But in many of the cases labor was easy, no instruments were employed and no visible damage sustained, yet the child develops wry-neck. In such cases it is assumed by Stromeyer that unrecognized and invisible injury has been

inflicted upon the sterno-mastoid muscle, into which hemorrhage occurred. With or without subsequent infection, as suggested by Mikulicz, the presence of the blood in the muscle, might occasion reactive inflammatory changes, with loss of muscular substance, formation of fibrillar tissue and shortening with resulting deformity. But under such circumstances the condition could not show itself until all of the implied changes had occurred, which must take considerable time. It could in no way account for cases in which the disturbance appeared at or shortly after birth. They must result from something antedating birth, and as not a few of the cases appearing at birth are found to be hereditary, for them, at least the determining condition must go all the way back to the germplasm. It may be that more cases have this origin than is generally supposed for upon careful examination, and comparison of the two sides of the face and cranium, it is not infrequently found that the wry-neck is accompanied by marked, though not immediately noticeable asymmetry of the parts.

FIG. 138.—Congenital torticollis. (*Meyerding*.)

Finally must be mentioned the probability that a few of the cases may be the result of crowding and malposition of the fetus in utero, resulting from deficiency of liquor amnii.

Asymmetry of the Pectoral Regions with Amastia

The young human embryo is provided with rudiments of many mammary glands which it receives through inheritance from its remote phylogenetic ancestors. It retains but two of them, extinguishing the superfluous ones.

It has already been shown that if more persist, polymastia, or excess of mammary glands occurs; if more are extinguished, there will be one or no mammary glands. Now it occasionally happens that a child is born with only one mamma and in such cases, the above given embryological explanation might be accepted, were it not for the fact that in almost every case it was not only the mamma that was absent, but also one or both of the pectoral muscles of the same side.

Froriep supposes the defect to be caused by the pressure of the arm of the fetus upon the side of its thorax while in utero. The theory seems to be consistent with the facts, for there are cases in which the mammary gland is present, but diminutive, and the muscles are present, but atrophic; there are cases in which the mammary gland is absent, and the major pectoral absent; there are cases in which the breast and both pectorals are absent, and others in which the breast, both pectorals and part of the deltoid are absent, and there is a case, reported by Thompson, in which the arm could be fitted into a groove in the tissues of the thorax, corresponding to the tissue losses.

It therefore seems as though the malformation might be the result of intra-uterine pressure, from deficiency of liquor amnii.

VI. DEPENDING UPON INJURIES INFLICTED UPON THE FETUS DURING BIRTH

Cephalohematoma

When the head of the fetus engages in the maternal soft parts preparatory to delivery, an area of scalp corresponding to the gradually dilating os uteri, being unsupported, yields to the distending force of the fluids that collect in consequence of the venous and lymphatic obstruction and rises to form a soft elevation, commonly known as a *caput succedaneum*, or *spurious cephalohematoma*. If, through any unusual circumstance, the position of the head is changed during labor, a second lesion of the same kind may occur on another part of the head. If the head is long delayed in the pelvis, it is said that a similar lesion may form over the area of the scalp corresponding to the position of an obturator foramen, so that the child may be born with two. But ordinarily there is but one, situated over a parietal eminence, where its occurrence is to be expected.

Such lesions are unimportant, and disappear a few days after birth, except when complicated by the presence of blood in the accumulated fluid, which delays absorption.

But the most interesting cases are those in which with or without the caput succedaneum, there appears, a few days after birth, a lesion much resembling the caput succedaneum, but dark in color, and obviously containing blood as the principle ingredient. This is known as the *cephalohematoma*, and occurs about once out of every 250 births. It is less easy to account for than the caput succedaneum, for though it corresponds pretty well with it in position, it differs in not appearing until several days after birth and in frequently making its appearance on some other part of the fetal skull than that presenting at the os uteri. It also may occur upon the heads of children that presented by the breech. In general, it is also more frequent over the right parietal bone, though it is the left that most commonly presents, and it not infrequently appears over the frontal or occipital bones. It forms a dark-colored swelling the size of a nut, rarely the size of a half orange, never, under any circumstances trespassing upon the tissues beyond the lines of the surrounding sutures, and never crossing from one to another of the bones of the cranium. It is soft and fluctuating, and cannot be reduced. Pressure upon its does not occasion any nervous or other important symptoms. It does not seem inclined to disappear, but persists for weeks, and after the second week develops a new sign, a distinct elevated bony ring that can be felt with the finger to surround a central opening or depression, beyond which palpation is difficult. This sometimes excites apprehension if it be mistaken for a central communication with the interior of the skull.

The explanation of the lesion is simple. It is a hemorrhage beneath the pericranium, separating the membrane from the bone. The absorption of the blood is slow, and in the meantime, the elevated pericranium, which is an osteogenetic membrane, continues its function where not too much disturbed, i.e., at the margins of the lesion, producing a ring of bone above the normal level, and thus giving to the palpating finger the impression of a central opening. Later, as the blood is absorbed, and the center sinks, the pericranium resumes its normal relations, and the function of osteogenesis continuing, the adventitious

ring of bone is resorbed and normal relations re-established. Except in cases
in which meddlesomeness has led someone to puncture the lesion, and thus
paved the way for infection, the lesion takes care of itself, and recovers perfectly
and with reasonable promptness.

But the source of the lesion, where no damage has been inflicted, is mysteri-
ous. The truth of the matter is that it does not occur where there has been no
injury. Traumatism is always at the bottom of it, though it is not always of a
character readily determined. It was Féré who first pointed out that if the
cranial bones of an infant at term be examined, numerous minute fissures
will commonly be found radiating from the centers of ossification, out-
ward toward the sutures. If pressure be made upon bones in this stage of
development, the fissures spread slightly, and the little blood-vessels by which
they are frequently crossed, rupture. Should the mechanical disturbances
consequent upon delivery act similarly, the same result may follow, and the
escaping blood collect beneath the pericranium, where it forms cephalohema-
toma.

VII. DEPENDING UPON DISEASE OF THE FETUS IN UTERO

Congenital Hydrocephalus

Hydrocephalus results from fluid distension of the ventricular cavity of the
brain, or of its sub-arachnoidian space. The former, which is common is
known as *internal hydrocephalus;* the latter, which is rare, as *external hydroce-
phalus.* When congenital it may be apparent at birth, or develop shortly after;
when acquired, it may occur at any time of life.

The present discussion, has particular reference to internal hydrocephalus
of the congenital and infantile form, but occasional references to the others will
be inevitable in order that the subject may be understood.

Hydrocephalus is of not infrequent occurrence, but varies at different times,
in different places, and in the experience of different men.

> von Winckel saw it 8 times among 15,000 births, or 1:1875
> Kleinhaus   saw it 1 time among 1,600 births, or 1:1600
> Merriman   saw it 1 time among   900 births, or 1:900
> Schuchard saw it 1 time among   753 births, or 1:753
> Göttingen Clinic   8 times among 4,200 births, or 1:525

In one year, in the Göttingen Clinic, 4 cases were observed, though only 8
cases had come under observation during the previous 20 years.

The acquired form of the disease usually results from meningitis—acute
cerebral meningitis, epidemic cerebro-spinal meningitis, tuberculous meningitis,
or basilar syphilitic meningitis. Sometimes it follows brain tumor, tyroma,
gumma, or other conditions accompanied by obstruction of the drainage system
of the brain, i.e., closure of the foramina of Monroe, the foramen of Magendi,
the aqueduct of Sylvius, the transverse fissures of the brain, and the lateral
recesses of the fourth ventricle.

The beginning of the congenital form of the disease antedates birth, but for different and unknown lengths of time. In some cases it is so advanced, and the head of the child so large that it cannot be born, or explodes during labor, or retards delivery so as to necessitate emptying the cranial cavity in order to effect delivery. In other cases the disease is so little advanced that the child is born without complication, and at first appears normal. Without definite knowledge upon which to base an opinion, it may be assumed that the larger the head at the time of birth, the longer the disease has existed, the accumulation of fluid is usually slow and progressive. In those cases in which the head begins to enlarge immediately after birth, it may also be assumed that the disease existed at the time of birth.

The appearance of the hydrocephalic child is so characteristic that there is no question of the diagnosis. Of course, it goes without saying that the more exaggerated the condition, the greater the ease of diagnosis.

The child has a head enlarged out of all proportion to the size of its body, and so heavy that it cannot move or lift it. The increase is entirely limited to the cranium which becomes very large and peculiarly globular through the obliteration of its various fossae. The temporal bones, for example, are no longer flattened or slightly excavated at the position of the temporal fossae, but round out into part of the general globe. The forehead bulges until it overhangs. The cranial bones are all widely separated, the sutures greatly widened, and the fontanelles of immense size. The orbital plates of the frontal bones are depressed so as to trespass upon the orbital cavities, and cause the globes of the eyes to protrude, and there being no secondary changes of the soft parts to compensate for the dis-

FIG. 139.—Congenital hydrocele. (*Weidman.*)

placement, the exophthalmos becomes so pronounced that the eyes cannot be closed, even in sleep.

Upon dissection it is found that the cranial bones have developed to the normal limit, though unable to inclose the enormously increased size of the cranium. They therefore appear thin, and the centers of ossification being widely separated and scattered, they seem to be imperfectly formed. Considerable extents of membrane occur without other than Wormian bones. The face does not participate because the distending force in no way acts upon it, but it presents a very peculiar appearance, which Shultze describes as

a kind of attached triangle, the apex of which is the chin. The scalp, espe-
cially of the temporal region, sometimes shows numerous large veins.

When the cranial coverings are removed, the cause of the distension is found
to be a collection of fluid enclosed in the ventricular cavity of the brain, which
may be distended out of all anatomical proportion and resemblance. The
chief dilatation affects the lateral and third ventricles of the cerebrum. Both
Ballantyne and Birnbaum speak of cases of extreme hydrocephalus in which the
brain was altogether absent, and the cranium converted into a skin-like sac filled
with fluid, with the scanty remains of brain substance lying at its base. Such
extreme degrees of distension and atrophy are, however, very rare, and it is more
common to find the cerebral substance reduced to a thin rind a few millimetres
in thickness, in which the differentiation of white and gray matter is no longer
clear. In most cases the cerebellum suffers little more than slight dislocation
of its various nuclei, but Chiari has found it atrophic or even absent in rare
instances. The basal ganglia, which suffer greatly from compression, retain
their functions until the extreme degree of disturbance is reached. That is
naturally much longer in the prenatal form of the disease where independent
action of the nervous system is less important than in post-natal life.

The fourth ventricle may not be disturbed, or may be displaced downward.

As the increasing fluid exerts its distending force, the cerebral cortex is
compressed between the fluid on the inside, and the cranial coverings on the
outside, and its convolutions are flattened, the temporo-sphenoidal lobes
obliterated, and the islands of Reil uncovered. The corpus callosum is elevated
by distension of the third ventricle, and the septum lucidum with the contained
fifth ventricle gradually extinguished. The falx cerebri and tentorium cere-
belli become smaller and smaller until they almost or quite cease to exist. The
optic chiasm is compressed, separated, and may disappear by atrophy, so that
blindness is inevitable.

The infundibulum may be deepened and widened. The spinal cord may
participate, and hydrorrhachis and hydromyelia occur. Not infrequently
there is associated spina bifida.

These extreme degrees of distension in hydrocephalus are only possible when
the occurrence of the disease precedes the completion of the bony cranium. If
it arise later, after the cranium is completed and its sutures closed, it does not
open the sutures again, nor does the head enlarge but the pressure of the fluid
distends the ventricular cavity and compresses the brain until its basal ganglia
are no longer able to continue their automatic functions. Under these cir-
cumstances the disease progresses without visible external signs, and apart from
the symptoms of compression of the brain from which the individual dies, does
not distinctly show itself until at autopsy an abnormally great quantity of
cerebro-spinal fluid escapes under pressure, from a considerably dilated ventricu-
lar space.

It is, therefore, only in the fetal and congenital cases that unlimited oppor-
tunity for cranial dilatation can occur, and its extent is almost beyond belief.
It is not improbable that when the disease sets in at an early period of fetal life,
the distension of the head becomes so great as to cause rupture in utero, and the

common and peculiar appearing monster described as *anencephalic* is supposed to be but the further bodily development of a fetus whose head and brain were previously thus destroyed.

The later occurrence of the trouble, may result in heads of so great a size as to be a serious impediment to birth, at which time they may rupture or be opened.

But in the greater number of cases none of these things happens. Either the child is successfully born with its enlarged head, or shortly afterward the head enlarges, and it continues to live on for months, the head growing larger, and sometimes reaching great dimensions. Anton saw a case in which the head measured 85 cm. in circumference, and contained 8300 cc. of fluid. Death then usually comes from compression of the centers, though it may occur more early from intercurrent pneumonia or gastro-intestinal disease.

In rare cases the children live, the fluid ceases to increase, the pressure symptoms abate more or less, and the head ceases to enlarge.

What then follows will depend upon the extent of the damage already done. The child may grow, but be paralyzed; if not, it usually soon becomes evident that it is unintelligent. It learns to walk, and moves about sluggishly balancing its ridiculously big head with difficulty, and scarcely learns to talk. At school no progress is made. Many cases live for years in this state, and most almshouses and insane asylums contain one or more such persons some of whom have reached middle life.

In a very few cases, although the head is visibly larger than it should be, there has been no damage to the intellectual centers, and of them a few notable exceptions have even attained to intellectual pre-eminence. Helmholtz, Cuvier and Menzel are all said to have been recovered hydrocephalics.

There seems to be no evidence that hydrocephalus is hereditary. Most of the cases die, and few of those that survive are capable of having offspring.

Of the few that recover and have families, no mention seems to be made of the appearance of the disease in their children.

But numerous hydrocephalic children may be born of the same mother. Frank reports a woman that had six hydrocephalic children, and another that had seven. Goelis also reported the case of a woman that bore six hydrocephalic children in succession. In such instances the occurrence of the disease in the children can scarcely escape being referred to the parent. Gaboil, who carefully considered the maternal aspects of the cases he examined, found that in many the mothers had recently suffered from pneumonia, small-pox, influenza tuberculosis, syphilis, or other infectious disease, any of which might be conceived to affect the fetus either directly through infection, or indirectly by intoxication. Fournier was of the opinion that maternal syphilitic disease was the great cause of hydrocephalus. It seems, however, that some cases occur where there can be no suspicion of specific disease. Some cases are known to have followed maternal injury during pregnancy, but it would be an egregious blunder to argue from them that all cases were referable to traumatism. To refer them all to syphilis may be as bad. When hydrocephalus occurs in association with other congenital malformations such as spina bifida, there is great temptation

to attribute them to the same general cause, but they may be quite independent of one another.

The etiology of the disease is therefore uncertain. It seems best explained on the assumption that fetal or infantile meningitis has occurred, and that the fluid collection began as inflammatory exudate, and continued as increasing transudation. It might be supposed that an examination of the cerebro-spinal fluid would make this clear, and sometimes it does throw light upon it. Thus, in a few cases the fluid is turbid, and upon microscopic examination shows abundant leucocytes. There is then no doubt about the presence of meningitis, but doubt usually arises as to whether the condition discovered be primary or secondary—in the latter, it of course offers no explanation of the hydrocephalus, per se. But in nearly all cases the fluid collected turns out to be very much like the cerebro spinal fluid itself. It is usually clear, watery, colorless, or very occasionally yellowish, contains only a trace of albumin, has a specific gravity of 1.001 to 1.009 and contains very few cells.

The difficulty is that the fluid cannot be collected or examined at the proper time. When the children are born the disease has usually existed for some time, and the acute inflammation long since ended.

It might also be imagined that the origin ought be elucidated through careful examination of the tissues at autopsy. If antecedent meningitis had occurred, signs of it ought to be found. They are constantly looked for, and claims both pro and con are made, but no concensus of opinion has been reached. Schultz observed that the surface of the ependyma is frequently sprinkled with fine granules, like grains of sand, and that in other cases there are fine reticula upon the basal parts of the membranes. These he regarded as sufficient evidence of antecedent inflammation, and deduced that hydrocephalus was always caused by meningitis. But it is by no means certain that the tiny granules he saw, are not similar to or identical with the *granulia* so common upon the peritoneum in acites, and so often mistaken for miliary tubercles. How mistaken one would be if from the discovery of their presence he would proceed to argue that ascitic collections in the peritoneal cavity must always arise from peritonitis! It is, therefore extremely difficult to determine the precise cause of hydrocephalus; it probably differs in different cases, but it seems certain that meningitis is the most common and important factor.

PART II

TUMORS

PART II

TUMORS

GENERAL CONSIDERATIONS

The word "tumor" is an ancient Latin one, the English equivalent of which is "swelling." It was originally applied to various "swellings" that later knowledge has shown to be more correctly placed among other morbid processes. Thus the sub-acute and chronic granulomas have been eliminated. Such subtractions naturally reduced the total number of lesions classified as tumors, but as the remainder have been subjected to searching histological investigation many new genera and species have been added so that the number of named tumors seems to have increased.

During the last quarter of a century, tumors have been much more scientifically studied in the laboratory than in the clinic, with the unfortunate result that more has been found out about their histological structure than about their clinical disposition. Diagnosis gradually passed from the surgeon and clinician, to the pathologist, with the erroneous supposition that the final word in diagnosis and prognosis must lay in the microscopic findings. This is unfortunate. The microscope only determines the finer structure of the tumor, and enables it to be classified. If it definitely fall into a well known group, the prognosis common to that group can be made with a reasonable degree of accuracy; but if it happens to be otherwise the pathologist may be left in uncertainty as to what its future behavior will be. It is true that from a certain type of structure a certain behavior may be predicted, but unless confirmation or refutation of his prognosis be received from the clinic, how can the pathologist escape multiplying his errors? He sees only the tumor; the surgeon sees the patient and to him only can it be known what eventually happens. Tumors declared harmless by the pathologist sometimes return and destroy the patient's life; others that he declared to be malignant never trouble the patient again. Many of the most important facts about the prognosis of tumors are still to be learned, but it can be done only by the earnest coöperation of the surgeon and the pathologist.

In the long run, the prognosis of a tumor is far more important to the surgeon than the diagnosis. In order to render a sound judgment upon that point, the pathologist must know how many other tumors of like kind have behaved, and that information he must derive from the clinic.

The average surgeon seems to suppose that when the removal of the tumor, has been skillfully accomplished, his responsibility is at an end. That is a mistake. His most important contribution to science will be the publication of his final results. Which of the tumors he removed came back? Why did they come back? Because of their inherent nature, or because of the inadequacy of the operation? Was the behavior of the tumor after operation as

predicted, or the reverse?　If the latter, why was the mistake made, and how can similar mistakes be avoided in the future?

The literature of tumors is largely made up of interesting case reports, detailing the gross morbid appearance of a tumor, the ingenuity of the operation, and the report of the microscopist, published but a few weeks or months after the operation was performed, and either telling nothing of the future of the patient, or, what is worse, informing the reader that the tumor did not recur, when the time elapsing between the operation and the time of the report, was too short to make the statement of any value.

Nothing but embarrassment and mis-information is to be expected from the mystification method of treating the pathologist adopted by some surgeons, who send specimens to the laboratory, intentionally suppressing essential information.　It may then be impossible for the pathologist to tell what they are or where they come from, so that all of the benefit the surgeon hoped to derive from the examination is lost.

A microscopic examination of a tumor is made for the purpose of *assisting* in the discovery of its true nature and disposition, and to this end, all of the clinical details should be placed in the hands of the pathologist, to facilitate his efforts in every way possible.　Not to do this, is an injustice, and places him in such a position that his opinion is of no value to his surgical colleague and may result in injury to the patient.

The writer is frequently besought by friends to assist them in the microscopic diagnosis of tissue sent to their laboratories without other data than the name of the patient from whom it was derived and the name of the surgeon by whom it was sent.　Under these conditions it may be possible to tell all that is desired, but it is just as probable that nothing at all can be found out.　When it is possible to make the diagnosis of a tumor by a glance at a microscopic section, it is usually just as possible to make it by an examination with the naked eye.

In these days of thorough training, it might be supposed that it is for the confirmation or refutation of his own diagnosis that the surgeon consults the pathologist, and that it is rather for the prognosis than the diagnosis that he seeks assistance.　If that be true he should exercise judgment in the selection of the material, sent for examination, and carefully note its relations and extensions, all of which he will report to his consultant.　Failure to do this sometimes results in the defeat of the very purpose for which the examination is made. Thus, a surgeon some time ago sent a piece of tissue, rounded in form, the size of a small pea, rough on the surface, and flattened at one point that was undoubtedly the line of the section by which it was removed.　With it came a polite note stating that it was removed from the skin of one of the sender's patients, and that he desired to know whether it was of benign or malignant disposition. After careful examination, the pathologist reported that it seemed to be a much inflamed papillary squamous epithelial growth, probably a wart, and that it did not show any definite signs of malignancy.

The surgeon failed to say that the lesion was one of a number of similar small excrescences formed about the edge of a crateriform ulcer with indurated

edges that he suspected to be a carcinoma. He therefore placed his consultant in the position of unavoidable but dangerous error. What the surgeon really desired to know was whether there was, as he believed, carcinomatous infiltration of the tissues about the base of the ulcer. How could that be determined from the examination of a superficial excrescence? Can anything but thoughtlessness excuse the surgeon for his choice of material? Yet he subsequently heaped ridicule upon the pathologist.

A less polite colleague once sent a perplexing specimen for microscopic diagnosis, and in answer to an inquiry concerning the source and probable nature of the material, answered that "if the pathologist had to be told what it was, it was clear that he didn't know, so needn't bother farther."

Another once wrote that "If he had known what the tumor was, he would not have asked."

To satisfy the average surgeon it is necessary to give every tumor a *name*. Now, the names of tumors are often makeshifts for temporary classifying and cataloguing for future and precise study. The names given to tumors also vary in different places, at different times, and according to the theory of nomenclature. A tumor of unusual structure is likely to be given different names by different pathologists, according to the different theories of origin they entertain.

For example: a microscopic section of a malignant tumor is shown to a French pathologist, and he makes a diagnosis of *cancer*. No English or American pathologist would agree, because a glance through the microscope shows a cellular tumor of connective tissue derivation, a *sarcoma*. Is this an egregious blunder? Not at all; the French pathologists call all malignant tumors cancers, so, according to the custom of his school our friend regarded this as a *connective tissue cancer*. The same section is later shown to other pathologists of our own country, and the first contents himself with calling the tumor *sarcoma;* a second thinks the cells arranged in a definite manner about an excessive number of blood-vessels and to him it is *angio-sarcoma;* a third notes that in one part of the section the cells immediately about the blood-vessels are arranged in an orderly fashion and in good health, while others are degenerating, and to him that means *perithelioma;* a fourth believes that the blood-vessels are the source of the cells of the tumor, and therefore to him it is an *endothelioma.*

Here, then, are five different diagnoses of the same tissue, all given by competent pathologists. It seems mystifying, but what will be the frame of mind of a novice if with the same section he makes a second round of visits to his acquaintances, telling them of the various diagnoses he has received, to learn from each that the others were quite correct, that all of diagnoses were fully justified, and that the matter of the name is of little importance anyhow?

There can be no uniformity of opinion as to what a tumor shall be called until it is more definitely known what that tumor is. At present it is not known what any tumor is.

The intensive histologic study of tumors has resulted in the naming of a great number of species not always justified by actual differences in their structure.

It is a mistake to suppose that any part of a tumor is always representative of the whole, and be content with the examination of a single fragment. Conclusions drawn from such superficial study are apt to be misleading. Every tumor should be cut in many directions, and each different appearing portion separately examined. The older center and more recent margins rarely correspond in structure; the well-vascularized and rapidly growing portions are usually quite unlike the older compressed, degenerated and necrotic areas.

The literature of tumors is enormous; it is also very confusing, no small part of the discouragement experienced by every student being due to the lack of uniform nomenclature and the lax use of terms.

If a tumor happens to be reported under a name for which there is no justification, it, of course, is likely to figure in all later synopses and tabulations of tumors bearing the same name, sometimes with the most contradictory results. Things by no means alike or related to one another are brought together and surprise is expressed that they behave so differently.

With the increasing employment of the X-rays and radium in the treatment of tumors, it has been found that certain tumors seem to be readily influenced by these agents, while others are not. Tumors sometimes appearing to be identical in structure differ in reaction to these agents. Why this difference? It is not yet fully determined.

Another must, therefore, in the future, coöperate with the surgeon and the pathologist in the scientific study of tumors, and the solution of their many difficult problems.

Before beginning the consideration of tumors it would be well to have a clear and scientific conception of what a tumor is. But in the present state of knowledge that is impossible. No one knows exactly what any tumor is, and therefore cannot define it except in the broadest terms.

After years of teaching, and the formulation and abandonment of many definitions, the author has finally settled upon the following as expressing what the term "tumor" means to him.

A tumor is a congenital or acquired anatomical defect, characterized by an excess of some tissue or tissues, fairly well circumscribed in distribution, atypical in structure or arrangement, subserving no useful purpose, and tending to increase and persist without respect to those influences by which the organic economy is maintained.

An analysis of the definition brings out the following facts;

1. *Tumors are congenital or acquired.*
    (a) Congenital. In the section of this work dealing with the Congenital Conditions of Surgical Interest, the reader will find descriptions of many tumors of congenital origin, some of which are evident at the time of birth, some of which appear later from rudiments existing at the time of birth.
    (b) Acquired. Most surgeons and pathologists are of the opinion that the greater number of tumors are acquired in postnatal life. Upon this matter, however, there is no definite information. All that can be said is, that the more carefully tumors are studied, the greater seems to be the number whose origin can be traced to abnormalities of embryonal life.

2. *They are anatomical defects characterized by an excess of tissue.* To the naked eye a tumor is a mass of tissue, and to the microscope it shows itself to be composed of cellular and intercellular tissue elements, for the most part readily classifiable histologically. In most cases there is resemblance rather than perfect correspondence between the tumor tissue and the normal tissue.

3. *Tumors are fairly well circumscribed.* It is the circumscription of the tissue mass that separates tumor from hyperplasia, but it is only the judgment of the observer that determines the distinctness of circumscription that shall characterize tumor. Some writers include such diffused hyperplasias as elephantiasis, dermatolysis and gliosis among tumors, others exclude them. There can be no satisfactory agreement until more is known of the origin and nature of tumors in general. Many tumors are not only well circumscribed, but are also encapsulated.

4. *The tissues of tumors are atypical in structure and arrangement.*

5. *They subserve no useful purpose.* These two statements are correlative. It may be partly because of their atypical structure and arrangement that they can subserve no useful purpose; it may be because they are without function that their structure is atypical. Isolated and circumscribed masses of fibrillar, osseous or cartilaginous tissue, can neither assist in the support of the tissues, or give rigidity to the skeleton. Nor can muscle cells perform any useful function unless arranged in bundles by which their contractile powers are made effective in relation to something to be moved. It might, however, at first seem as though a tumor composed of a circumscribed mass of adipose tissue, such as makes up a lipoma, might subserve the usual function of adipose tissue, and store reserve food against a time of future necessity. But although this tumor stores up the reserve material, it is not in the interests of the body generally, for when the time of need arrives, and the fats must be drawn upon, the tumor refuses to give up its reserve, and may continue to increase its stored deposit, though the body, as a whole, is emaciating.

6. *Tumors tend to increase and persist.* Inflammatory enlargements, which are frequently mistaken for tumors tend to increase only so long as the irritation continues, then subside; tumors continue to grow. It is a rare thing for a tumor to diminish in size, and almost an unknown thing for it to disappear. When it happens there is usually some explanation for it. Thus, a submucous fibroid of the uterus, subjected to the muscular contractions of the disturbed organ in which it occurs, may be squeezed out of its bed, and eventually delivered to the exterior of the body, thus terminating its existence. Or, a nasal polyp with a slender pedicle may be torn loose through violent blowing of the nose, and discharged from the body. Or, a tumor with a slender peduncle may suffer a twist that closes its vessels, and causes its tissues to die from starvation and become absorbed. These are accidents and vicissitudes of tumor existence, and only exceptions to the rule. Condy-

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loma acuminatum, the venereal wart, and verucca vulgaris, the common wart are known to disappear spontaneously, and are often cited as examples of recovering tumors; but it is doubtful whether they are tumors, for it is well known that the former arise in consequence of venereal infection, to disappear as it recovers, and the latter have recently been shown to be communicable by inoculation with a needle dipped in a filtered extract of a similar lesion. Both are, therefore, infectious diseases, and not true tumors.

But the question of satisfactorily separating tumors and infectious diseases is a difficult one. Many regard tumors as independent of infection or inflammation, and should a microorganism be shown to cause one, would immediately transfer it from the class of tumors to that of the infectious diseases. This is, indeed, our own attitude. But there are others who suspect that all tumors will ultimately turn out to be infectious in nature, yet remain in a class by themselves because of the dissimilarities between them and the other infectious diseases.

7. *The tumor is independent of the influences by which the organic economy is regulated.* Fractures of bone are supported, during the period of repair by a peculiar atypical osteoid tissue known as provisional callus. It forms a fairly circumscribed mass much like a tumor, but is temporary, and disappears as its usefulness comes to an end. Clearly its formation and transformation are parts of a well regulated regenerative function. No temporary function can be ascribed to tumors. The tissue develops where it is not needed, increases for no valid reason, and in obedience to no fixed law. From the very beginning it assumes an independence that makes it parasitic, and an individuality that cannot be reckoned with. Some tumors grow so slowly as to seem unchanged; some grow by fits and starts; some grow slowly and persistently, some rapidly and continuously. The best that can be said is that the greater number of tumors of the same kind behave with fair uniformity. No necessity of the body as a whole seems to affect them. The body may be starving, but the tumor keeps on growing. A possible exception is seen during pregnancy, when cancers are said to cease growing temporarily, but in many cases they seem to make up for the time lost by more rapid subsequent growth.

Fundamentally different conceptions should be associated with the terms *hypertrophy*, *hyperplasia*, and *tumor*. Carelessness in their employment results in confusion, and in bringing together things essentially different. As the words must be frequently used in the subsequent text, it will be well to begin by defining them as accurately as possible.

Hypertrophy.—This is derived from two Greek words, ὑπερ, over, and τροφή, nourishment. It is defined by Webster as "overgrowth or excessive development of an organ or part; an increase in the bulk of pre-existing normal elements."

If some of the cases to which the term can unequivocally be applied be considered, it will be found that in hypertrophy the general configuration of the part

or organ is not disturbed, and the relation of its components unaltered. It is sometimes described as symmetrical enlargement. Classical examples are the enlargement of the heart in compensating for valvular defects, enlargement of the uterus during pregnancy, and enlargement of the mammary gland during lactation. In each of these cases the respective organ undergoes enlargement, but preserves its histological arrangement. It might be said that the histological appearance of the mammary tissue is transformed, but upon analysis it will be found that though there is a great increase of the glandular substance, and its individual units are distended by secretion, the essential structure is preserved.

If an entire gland or other organ undergoes enlargement through increase of its essential structure, without important histological alteration, as is so often the case with the thyroid and the pituitary, the condition is hypertrophy, and not tumor. The same is true of the prostate gland, whose enlargements, sometimes described as adenoma, are more frequently and correctly called hypertrophy, except in the somewhat unusual cases in which there are localized circumscribed areas, upon whose presence the enlargement depends.

It makes no difference to what size the enlarged organ attains; if the essential structure be preserved the condition is hypertrophy. This is exemplified in cases of enormous hypertrophy of the mammae which may grow to a weight of 50 pounds or more.

Hyperplasia.—This word is also derived from the Greek, ὑπερ, over, and πλάσις, moulding. Webster defines it as, "an increase in, or excessive growth of the normal elements of any part, depending upon the formation of new elements." Scott, in Gould's "Practitioner's Medical Dictionary," makes it synonymous with numerical hypertrophy. Gould, in his "Illustrated Dictionary of Medicine," says that it is "an excessive deposit or augmentation of the elements of tissue composing an organ."

FIG. 140.—Elephantiasis of enormous development ("Barbadoes leg"). The condition is not a tumor. (*After Smith.*)

The exact difference between hypertrophy and hyperplasia is, therefore a very nice one to make, but seems to lie in the fact that in the latter, the increase in size depends upon the increase in the number of tissue elements, regardless of their essential histological arrangement. Any of the elements may increase in number without reference to any others, and the result may be disproportion and deformation as well as destroyed or diminished function. But it is also to be noted that the tissue that increases must be normal to the part.

Tumor.—Referring to the original definition, it will be seen that in tumor the tissue increase may be of some kind having no place in the organ in which

the tumor occurs, that it is totally devoid of function, and that it pays no reference to proportion or symmetry.

It is thus apparent that tumor and hypertrophy ought not to be confused with one another, that hypertrophy and hyperplasia ought usually to be fairly distinct, but that hyperplasia and tumor are in some cases only to be separated by the circumscription that is one of the chief characteristics of tumor. Beyond this it is impossible to go because some tumors are, in reality hyperplasias— cancers being among such tumors.

It seems well to think of a tumor as beginning at a minute focus; starting, as it were, from a single cell or group of cells, and increasing in size through multiplication of the particular elements concerned, without further reference to the tissue or organ in which they appear. There seems to be no ground for assuming continuous transformation of normal tissue into tumor—no successive beginnings. The tumor starts from some minute and undiscovered beginning, and immediately assumes independence and individuality, thrusting aside or forcing its way into the adjacent tissues not belonging to itself. The normal structures are not transformed into the tumor, but displaced or replaced by it.

With this conception of minute beginning, immediate individual tissue segregation, independent vegetative activity, and inutility in mind, it is well to inquire from what the tumor has its beginning.

The something from which the tumor develops, being unknown, may best be called its *primordium*, and concerning it the following conjectures have arisen:

I. The tumor primordium may be something entirely foreign to the body of the individual in whom the tumor develops,—as a parasite.
 A. It may consist of tissue from some creature of entirely different kind, implanted into him by accident.
 B. It may consist of tissue of another of his own kind, included in him by accident.
II. The tumor primordium may be indirectly foreign to the body of the individual in whom it appears.
 A. Having its origin in dissociated blastomeres.
 B. Having its origin in parthenogenesis of germinal cells.
III. The tumor primordium may be native to the body of the individual in whom it occurs.
 A. Having its origin in residual embryonal substance.
  1. In persisting vestiges of embryonal structures that should normally disappear by atrophy.
  2. In the undeveloped excessive embryonal cellular substance, of which all of the tissues of the body contain some.
 B. Having its origin in developmental defects.
  1. Hemartia.
  2. Chorista.
 C. Having its origin in the normal cells of the part in which it appears.

The first of the theories, that the tumor primordium is something entirely foreign to the body of the individual in whom it occurs, and may consist of tissue from some creature of entirely different kind implanted into him by acci-

dent, is almost too fantastic to merit attention. It is based upon the separate and independent nature of tumors, and upon occasional dissimilarity between their tissues and those of the host. The source of the implantation is supposed to be embryonal substance of lower creatures admitted to the body by ingestion —in the form of eggs partly developed,—or by transportation to abrasions of the surface of the body by insects that have recently visited torn and mutilated embryos of lower animals, whose cells have adhered to their limbs and bodies. The proponent of this theory supported it by the test of specific precipitation. Believing that the common fowl was the principal source of the implantation because of the frequence with which its eggs are eaten raw, he tested an extract
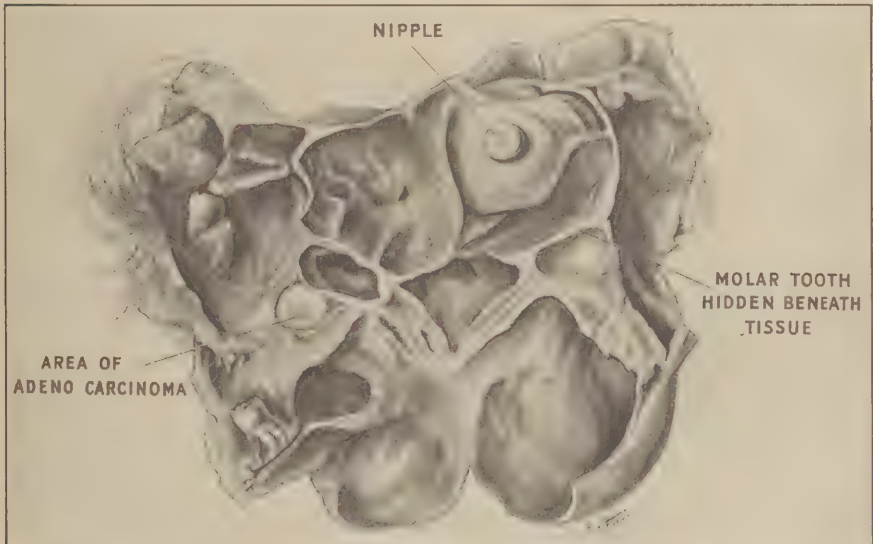
Fig. 141.—Dermoid cyst of the right ovary, containing teeth, hairs, a mammary gland and a small carcinoma. It was in two separate parts supposed to represent two separate original cysts and was unusually thin-walled. It is a teratoma. (*C. C. Norris.*)

of a spindle cell sarcoma, and found that it gave a precipitate with hen's blood serum. The possibility of such an origin for the tumor primordium is entirely contrary to the well-known facts regarding tissue implantation and grafting. Success is only possible when the tissue transplanted and the recipient of it are of the same species, or at least of the same genus of animals.

When the second proposition is reached, and the tumor primordium is conceived to arise through the inclusion within the individual of tissue derived from some individual of his own kind, a more reasonable basis of argument is discovered. From one egg, two separate, identical individuals, homologous twins, may develop; or, the twins, which arise through separation of the equally valent primary blastomeres, may be partly connected—conjoined twins;—or, the bodies of the conjoined twins may be partly blended; or, they may be intimately blended and their organs and tissues confused; or, one of them may outgrow its fellow and include it—embryoma—as a tumor-like formation. Such tumors

usually at once reveal their nature through the presence of recognizable organs or members, or may show a confusion of tissues not easily accounted for upon any other hypothesis.

Similar tumors may be accounted for by a different theory. Thus, the dermoid cysts and tumors of the ovary, although they contain a variety and confusion of tissues that makes it quite certain that they must represent some other individual than the host, occur so regularly in the organs that are the recognized depository of the germ cells as to make them the probable source. Now it is generally recognized that all of the germ cells do not reach the reproductive organs—a few are lost by distribution and become sequestered in other and sometimes remote parts of the body. Should these behave as similar cells normally placed in the ovaries and testes occasionally do, and attempt parthenogenetic development, a confusion of miscellaneous tissues and suggestion of organs may result, and a kind of tumor form. In this case the primordium is not strictly speaking derived from the individual in whose body the tumor grows, but from the germ plasm of which he is the custodian. It is in this sense that the tumor is only indirectly derived from his tissues.

When those cases are reached in which primordium is conceived to be native to the body in which it grows, and the tumor, therefore a part of its own substance, new difficulties are encountered.

FIG. 142.—A collection of adipose tissue in the wall of the uterus. The magnification is too low to permit histological details of any of the tissues to be discovered, but the pale area is adipose, all the remainder unstriated uterine muscle.

The unfinished, imperfect character of the tissues of many tumors, and their remarkable disposition to grow, suggest residual embryonal tissue as the primordium. A survey of the body with this thought in mind, shows many points at which vestiges of embryonal tissue sometimes survive, and at which tumors occasionally arise. So much is said about this phase of the subject in the section upon "Congenital Disturbances" that it is not necessary to repeat it here. It is certain that a number of tumors arise from vestiges of embryonal tissue surviving at definite points in the body, where the developmental processes were complicated. In a few cases it is clear that the tumor arose through disturbances of embryonal development, as where an organ fails to appear, and its place is taken by a larger or smaller mass of nondescript tissue resembling a tumor—the *hamartia* of Albrecht—or, where in the development of the organ, fragments of its rudiment become separated from the general mass, to complete their development, as well as they could, in some new environment, with resulting supernumerary or accessory organs, or distributed bits of tissue recognizable as intended parts of organs—the *chorista* of Albrecht. Need it be said that neither a hamartia nor a chorista is a

tumor? It is a developmental defect, a malformation. Such choristas are frequently referred to as Cohnheim's "embryonal tissue rests," but seem not to be what that great master had in mind at all. In the first place they are not embryonal; they have developed and differentiated, and are as distinctly adult as any integral part of the organ to which they were intended to belong.

But if it is not these bits of adrenal tissue sometimes found in the kidney, on the spermatic cord etc., or the bits of pancreas found in the wall of the stomach and beneath the capsule of the spleen that constitute the material Cohnheim referred to, what were his "embryonal rests?"

The best way to answer this is to read what Cohnheim himself says about them:

"If you ask me wherein the abnormality in the disposition of the embryo that becomes the starting point and cause of a tumor consists, I can only answer with hypotheses. The simplest view appears to me undoubtedly to be that in an early stage of embryonic development more cells are produced than are required for building up the part concerned, so that there remains unappropriated a quantity of cells—it may be very few in number—which owing to their embryonic character are endowed with a remarkable capacity for proliferation. Anyone who more closely considers this hypothesis will, I believe, be led involuntarily to refer the production of superfluous cells to a very early stage, possibly to the developmental period between the full differentiation of the layers of the blastoderm, and the complete formation of the rudiments of the individual organs. So at least we shall, I believe, most easily understand why this abnormality gives rise later on, not to general hypertrophy of a part, but simply to a histoid tumor, i.e., to excessive growth of one of the tissues of the part. Moreover, it is possible that the superfluous cellular material may be more or less evenly distributed over one of the histogenetic rudiments or remain confined to one spot. In the latter case, the local rudiment of an organ, or only a definite region of the same, would subsequently become involved in the tumor formation; in the former on the contrary, the rudiment of an entire system, e.g., the skeleton or the skin, would take part in it. You will not, however, attach more importance to this view than can be fairly claimed for it; it is only a modest attempt at formulating somewhat more intelligibly the hypothesis of an embryonic disposition. Owing to our imperfect knowledge of the details of the process of growth, we are unfortunately still compelled to have recourse to guesses; but I put no value on the formulation itself, and am ready at any moment to exchange it for a better. The only point on which I lay stress is that the real cause of the subsequent tumor is to be sought in a fault or irregularity of the embryonic rudiment. . . . We do not claim that the tumor itself is congenital, but merely that its rudiment is; viz., we assume, in accordance with the view formulated by us, the existence of an excess of cells as compared with the physiological standard, out of which excess a tumor may ultimately develop. Thus, an extremely small, and scarcely perceptible nodule of the skin or subcutaneous fat, or of a gland, may, later on give rise to a bulky fibroma, lipoma or adenoma; an insignificant pigmented mole may become the starting point of a large melanotic growth, and a small cutaneous cyst that completely escapes notice develop into a dermoid of large size. Still more, it is quite conceivable that the cell clusters representing the rudiment of the tumor may be absolutely indistinguishable from the physiological elements of a part, by any means at present at our disposal. To distinguish them is not difficult when such abnormal cell groups are present in a dissimilar tissue, as, for example where islands of cartilage persist in the midst of fully formed bone. . . . But how will you determine from the appearances of a group of epithelial cells, of cells of the lymphatic glands or of the bone marrow, whether or not they are embryonic survivals? . . .

This is indeed by far the most common antecedent to the development of a tumor. The new-born infant brings with it into the world, not the tumor, but merely the superabundant cell material, and from the latter, if circumstances be favorable, a tumor may grow later on. I wish once more, however, to warn you against adhering too closely to the expression "superabundant cell material;" it would be perhaps more correct to speak of a material having an

inherent potentiality for subsequent tumor development. For the development of the tumor depends on this power, which for the rest is simply the quality so very commonly manifested in individual instances of inheritance and development."

From this it is evident that Cohnheim had in mind a primordium that might be collected and visible, or distributed and invisible, distinctly embryonal in character, and in no manner to be confused with the organically perfected choristas so commonly referred to as his "rests." So urgent is he upon the matter of the embryonal nature of the primordium that his very definition of tumor—*an atypical new formation starting in an embryonic rudiment*—hinges upon it.

But the most widely held theory of the tumor primordium, is that it is no other than the once normal, fully developed and well behaved tissue of the body itself, induced to grow into the tumor through abnormal circumstance.

With the exception of the first, which was only introduced to emphasize the peculiar isolation and independence of some tumors, these theories of the primordium are all valid, and with respect to certain tumors all are true.

The next fundamental question in regard to tumors is *why they begin to grow.*

If the tumor primordium be normal fully developed tissue, it is certainly a remarkable thing that, of a sudden and at a definite focus, a few of its cells should begin to grow and form a separate mass; if it be indistinguishable distributed embryonal cell substance, it is no less remarkable that it should begin to multiply at some point, and not over the entire body at the same time; if it be a chorista, or a vestige resulting from the survival of some embryonic structure, what induces it to grow after years of quiescence? If it be a germinal cell, why should one behave so differently from the others? It may at first seem sufficient to say that it is like embryonal cells to multiply, or that it is like germinal cells to germinate. But, as a matter of fact, it is not. And, furthermore, it is not generally conceded that the tumor primordium is either embryonal or germinal material. Whether, therefore, it be germinal, embryonal or differentiated adult substance, something underlies, initiates, and probably maintains the abnormal growth. What is it? It seems impossible to speak of it by any other name than a *stimulus*. But it must be a very local one. If it were disseminated throughout the blood, it must act upon many parts equally, and ought to cause hypertrophy, or the simultaneous development of many tumors. But multiple tumors are rare. It seems, therefore to be local and operative only at the focus at which the tumor begins.

After pathologists ceased to think with Abernethy and Hunter that tumors resulted from the organization of exudations from the blood, or with Broussais, that they were the consequences of repeated inflammation, and became acquainted with their cellular structure, this necessity for a cause of tumor development became acute. Virchow conceived it to be the irritation of traumatism, but about the time that his work became popular, a new idea was injected into medical science in the form of the "germ theory of disease." Nothing seemed better able, upon theoretical grounds, to explain tumor origin than the presence of a microörganism, and investigation of the subject from that point of view was at once begun and has continued until the present time.

The theoretical adequacy or inadequacy of the infectious origin of tumors is greatly complicated by the diversity of tumor structure. What might be regarded as supporting its probability with regard to one kind of tumor, cannot be similarly applied in the case of some entirely different kind of tumor.

As each successive period of investigation arrived, tumors were carefully investigated, first for bacteria, then for protozoa, then for yeasts, then for spirochetes, but always with disappointing results. Microörganisms of all these kinds were occasionally found, but only as accidentally present entities, and not as essential ones. Even arthropods have been suggested as initiating the tumor stimulation, and mites have been found in cancers under circumstances supposed to be incriminating. But no proofs having been adduced, the whole theory has been largely abandoned, and is commonly regarded as a kind of *ignus fatuus* that has led away from the truth.

Still, some stimulation seems essential and it becomes necessary to see if it may be of some other kind.

Traumatism, or injury, has long been regarded as the probable cause of tumor growth, and the number favoring this theory seems to be increasing, especially among surgeons. The subject is exceedingly difficult to discuss intelligibly or systematically because of the variety of injuries to be considered, and the restricted effects supposed to be produced by each. Perhaps it will not be amiss to begin the subject by pointing out that in estimating its importance too little attention seems to have been attached to the negative side of the question; no one seems to have been impressed by the fact that innumerable traumatic injuries are inflicted every day upon human beings who never suffer tumor development in consequence.

The greater number of observations and experiments upon irritation as the cause of tumors resolve themselves into a search for the cause of cancer, and thus rather lead away from the subject in general by dealing with a part of it in particular. This is all the more important to keep in mind because of the differences that separate cancer from other tumors.

Of all the lesions classified as tumors, cancer is most *sui generis*. It is on this account that the infectious theory of its origin has seemed so promising and been so industriously pursued.

Some might be disappointed, but few pathologists would be surprised if definite proof of the microörganismal nature of cancer were forth-coming tomorrow. Almost without exception the observations and experiments upon the conditions that lead up to cancer, have to do with infectious, inflammatory, parasitic, toxic, radiant, and traumatic injuries by which the admission of an infectious agent would be facilitated, and by which its entrance might be explained. It is doubtful whether in a single case the occurrence of the cancer can be traced directly and immediately to the effect of the agent investigated.

For the time being, therefore, the reader must observe that the discussion becomes confined to the primordium of cancer, and the agent that acts upon it. To the more general subject return will be made later.

The most successful experimental production of cancer is found in the work of Febiger who discovered that if the larvae of Spiroptera neoplastica (Gongy-

lonema neoplastica) were fed to rats, 53% of them, after an interval of 45 to 66
days developed carcinoma of the stomach.

That the tumors were real carcinomas there seems to be no just reason to
doubt as they were metastatic to the lymph nodes and eventually to the lungs.
This worm is common in the tropical countries, especially in the West Indies
and South America.   It has a double life cycle, living as an adult in the rat and

FIG. 143.—Gastric carcinoma in the rat, caused by infection with Spiroptera.   (*After Febiger.*)

mouse, and as an embryo in the cock-roach.   He also found that by depositing
the embryos upon the tongue of rats, it was possible in a much smaller percent-
age of the cases to induce cancer of that organ.   The question of chief interest in
these experiments is the relation of the worm to the induced cancer.   Can it be
said that it is the cause of the tumor?   Evidently not.   In nearly half of the
cases it only produced an inflammatory reaction, and the tumors were preceded
by inflammation.   Evidently the parasite does something that indirectly
results in the development of the tumor.

Probably next in importance is the well known observation that cancers of
the skin frequently develops upon the hands and arms of those that work with
coal tar and paraffine.   This has been put to experimental test by Yamagiwa,
who rubbed the inner surface of rabbits' ears with coal tar every two or three
days for long periods, with the result that massive epithelial overgrowth with all
the histological and clinical characteristics of skin cancer, including occasional
metastasis resulted.   As nothing of the kind is known to occur spontaneously in
rabbits, coincidence is out of the question.

Further proof of the same thing resulted from experiments performed by Tsutsui upon 259 mice, whose backs he painted with coal tar, with the result that 16 developed skin carcinoma, and one sarcoma.

The latter experiment seems to be of particular interest as indicating that there is a close etiological relationship between carcinoma and sarcoma. But in regard to both experiments the same question arises. Did the coal tar cause the cancer? And the answer must be the same, probably not. It only produced the inflammatory reaction by which the door was opened and the real factor called into action.

The livers of rats infested with the larvae of Trichosoma hepaticum and Taenia crassicollis not infrequently react by the formation of considerable fibrillar tissue, which sometimes assumes a cellular quality and resembles sarcoma.

At this point it may be well to call attention to a factor that must be considered in all experimental studies, namely, the inherited predisposition of certain families of rats and mice to the spontaneous development of tumors. Attention was first attracted to this, through the breeding experiments of Maude Slye, who, working with white mice from various sources, inter-bred those among which occasional tumors were noted, and kept separate the families in which no tumors appeared. After many generations of this careful artificial selection which was followed by more than 10,000 autopsies, and the discovery of 722 tumors of various kinds, it was found that no tumors appeared in families bred from no tumor stocks, while so many arose in the tumor stocks, that their incidence rose almost to 100%, and the tumors that appeared were quite regularly of the kind peculiar to the family, and in situations corresponding to the family tendency.

Can the predisposition to tumors evidenced by these mice be the result of tumor primordium inherited in such excessive quantity as to make tumor occurrence easy? Can miscellaneous irritants easily effect the occurrence of tumors in animals or men predisposed by inheritance?

Does the thought not lead again to Cohnheim's idea of a primordium consisting of superfluous cellular embryonal material? What would be so likely to be inherited?

But the list of tumors for which an irritative origin seems assured has, thus far only been touched. It must be explored more deeply.

It has been recognized for many years that the skin when exposed to the irritation action of soot is prone to develop squamous cell carcinoma, and the cancer of the scrotum so often observed in chimney sweeps, is known as "chimney-sweep's cancer." It is remarkable because the patients are usually much younger than cases of cancer are expected to be.

Nearly all writers have called attention to the cancer of the lip that seems to be so frequent among those who smoke clay pipes. The occasional occurrence of squamous cell carcinomas in the lesions of chronic lupus vulgaris of the skin, and upon the scars of burns, is well known. Indeed one particular form of skin cancer is known as "kangri cancer" because it so frequently follows the burns resulting from the too close application of the "kangri," or earthen pot filled with coals that Asiatic shepherds carry beneath their clothing to keep them

warm in the Himalayan highlands at night. Falling asleep under the influence of the pleasant sense of warmth, they are frequently burned, and for some unknown reason, it is said that these burns are particularly prone to develop into carcinoma of the skin.

Cancer of the cheek and tongue frequently occur in those with sharp carious teeth by which the tissues are continually irritated. Cancer of the stomach is now thought by many surgeons to have its origin in preceding ulcerations, and cancers of the duodenum are explained upon the same basis.

Cancer of the gall-bladder and bile ducts is so commonly associated with the presence of calculi, that many look upon them as resulting from the traumatic injuries inflicted by the stones.

Less frequent in exciting cancer, but occasionally undoubtedly having such result, are the eggs of the Schistosoma hematobium which, in the capillaries of the urinary bladder, first effect ulceration of the tissues, then the appearance of papillary and polypoid excrescences, which eventuate in cancer.

Many surgeons and pathologists now think they see cancer of the colon and rectum originate in small diverticula in which minute masses of fecal matter collect, exciting inflammation extending over prolonged periods, and eventuating in cancer.

Cancer of the neck of the uterus is far more common among women that have suffered traumatic injuries of the part during parturition.

Careless exposure to the X-rays has been the cause of squamous cell carcinoma of the hands of many of the earlier Roentgenologists, some of whom died in consequence.

It is not unusual for squamous cell carcinoma to develop at the edge of an old leg ulcer.

Here then, are the irritative conditions that have been determined by sufficiently repeated occurrence, to seem to lead up to cancer. But in no case can it be said that the agent immediately caused the cancer. It did something to the tissues, and cancer sometimes resulted, but in most cases it does not lead to cancer, but to a simple inflammation.

When attention is directed to the other variety of malignant tumor, sarcoma, it will be found that the connection between the growth of the tumor and the observed injury is even less clear. The most important contribution upon this subject seems to be that of Coley who among 970 cases of sarcoma, was able to find a distinct history of traumatism in 225, or 23%. In nine of the cases the tumor made its appearance a week after the injury, and in 117 within a month. The nature of the traumatism supposed to predispose to sarcoma is interesting. In most cases it was a contusion, and in most instances it was not destructive. Destructive, crushing and lacerated wounds rarely result in sarcoma. But other forms of traumatism may play a rôle. One sometimes sees a sarcoma develop at the edge of an ulcer, and experimental sarcomas have arisen in a few instances where X-rays had been frequently applied to the skin of rats.

But one should thoughtfully note, in passing, that at least 75% of sarcomas show no history of antecedent trauma.

When the group of benign tumors is considered, the cases in which the origin of the tumor can be referred to trauma become so rare as to scarcely merit mention. The subject may, therefore, be dismissed with the simple statement that traumatic injure seems to play no rôle in their occurrence.

From all this, it may be concluded that in about 25% of tumors some kind of trauma precedes the actual appearance of the tumor, and may play a part in its origin by furnishing the necessary stimulus to make its cells grow, though in 75% no such influence can be found.

But, supposing that in all cases a definite stimulation could be found, how does it act upon the tumor primordium? Is it through augmentation of the blood supply with resulting hypernutrition and vegetation? Is it by an auxetic action i.e., chemical excitation to rapid multiplication? Or is it the result of physical dislocation of certain cells that in a new environment vegetate luxuriantly?

It is not necessary that the factors act separately, they may do so in combination, but it is necessary to think of them as separate in order to weigh the probabilities.

The idea that the trouble lay in the physical dislocation of the cells into an abnormal environment originated with Ribbert who sees in it the very foundation of cancer. He conceives that the different tissues have their affinities and repugnances, and in their normal arrangement obey laws based upon these, maintaining what are regarded as normal boundaries. If, as the result of injury, cells of one kind are dislocated and thereby lose the restraining influence of a normal support, they may vegetate indefinitely. He thinks that cells of the epiderm thus separated from their fellows, and introduced into a damaged and non-resisting connective tissue, or the cells of glands thus dislocated into a stroma of diminished resisting power, may lawlessly multiply with resulting cancer. The theory is, of course, only applicable to cancer, and is not a general theory of tumor origin.

One theory supposes that excessive and phenomenal vegetative capacity of the primordium is at the foundation of tumor development. Another that the cells of the primordium may undergo conjugation, as the free cells of certain protozoa do, and thus acquire rejuvenation, followed by unlimited vegetative powers. Without evidence either for or against these theories, they merit no further attention. Still another theory is based upon the observation that tumor cells, and especially cancer cells, occasionally have but the reduced number of chromosomes, as though they were preparing for fertilization, and then began to multiply as the spores of some of the lower creatures do. But as the number of chromosomes is inconstant, it seems not to be important and, though its meaning is not understood, cannot be regarded as the starting point of tumor.

The most striking peculiarity of the tumor cell as contrasted with the normal cell is its unlimited vegetative power. Normal embryonal cells show no evidence of this capacity, but behave according to inherited impulses of phylogenetic origin. They multiply rapidly at first to produce the rudiments of all the organs and tissues, then, having accomplished that purpose, multiply slowly during the long subsequent period of growth, and with the perfection and

differentiation of the body structure, become quiescent. In many of the lower animals new growth taking the form of regeneration, or new formation of destroyed parts can be aroused by injury. But here again, though the capacity for growth seems to be almost unlimited—it will be remembered that Spalinzani saw a salamander regenerate its four limbs and tail five times, thus producing more tissue than was equal to the total weight of its body—it is always regulated according to fixed rules, and never results in aimless, continuous, and unlimited proliferation of tissue. Continuous growth appears upon more careful investigation to be no more a quality of embryonal than of adult tissue.

Tumors are divided into two classes according as their structure does or does not correspond with that of the tissue or organ in which they occur. When there is reasonable correspondence, the tumor is said to be *homologous;* when there is none, *heterologous.*

Homology between the tumor tissue and that of its nidus, has been supposed to indicate that in such cases the tumor primordium was the normal tissue; heterology, that it might be embryonal dislocation and inclusion. But in neither case does this necessarily follow; in the former it does not exclude Cohnheim's hypothesis—it will be remembered that he discusses this very point—and in the latter there may be another explanation, in the transmutation of tissue through the process known as *metaplasia.*

According to the dictionaries of medicine, metaplasia means "the transformation of one kind of tissue into another kind without the intervention of embryonal tissue." The transformation never exceeds the limits of blastodermic derivation. That is, connective tissues being of mesoblastic origin, never transform to epithelium, or epithelium which is of epiblastic or hypoblastic origin, to connective tissue. Examples of metaplasia are to be found apart from tumors, and should be carefully considered before an attempt is made to apply the principle to tumors.

Thus, calcification followed by bone formation is sometimes seen in traumatic injury of the muscles of the legs such as occurs in cavalrymen from contact with the straps and buckles of the saddle, and in the pectoral and deltoid muscles of infantrymen from contusions effected by the rifle in drilling, and in the chronic disease of the muscles known as *myositis ossificans.* It also occasionally occurs in the walls of blood-vessels, and in the chronically thickened valves of the heart, and rarely in scar tissue, and inflammatory exudates.

Metaplasia is commonly said to result from loss of specialization. The cells are supposed to proliferate so rapidly that differentiation is impossible. But this could account for no other circumstance than the return of the cells to what might best be described as an indifferent stage or appearance, and not for a change of type. Hansemann supposed that metaplasia was preceded by *anaplasia,* that is such rapid multiplication, that all differentiation was lost, the indifferent stage reached, and return to a kind of embryonic state brought about. The inherited tendencies of the cells thus lost, their subsequent differentiation took place along new lines.

But how else can metaplasia be explained? It might be done by an application of Cohnheim's principle of excessive embryonal cellular substance for if

he is right, and the excess occurs at a very early period of embryonal develop-
ment, and before the organs and tissues are differentiated, there is no reason why
primordial cells of various kinds and potentialities could not be distributed
among the developed cells, to give rise at any future time to tissue of some other
type. If the new formation was limited in amount and distribution, it would
correspond with the requirements of metaplasia, if circumscribed and excessive,
to a tumor. As the limb buds of the embryo, as well as its sclerotomes and
various of its segments contain cells, not originally separated or systematized,
from which fibrillar, chondrous, osseous, muscular and other tissues are to be
formed, it seems by no means impossible that some or many of them might be
more or less diffused and some sequestered, as embryonal development is
completed.

But it may not always be necessary to go back to the embryo to find an
adequate explanation for every metaplasia. In some cases the phenomenon
may be of more recent origin. Morley, for example, thinks that the bone forma-
tion in myositis ossificans is the result of the migration of osteoblasts into the
damaged muscles from the adjacent periosteal tissues. Traumatic injury
with subsequent inflammation certainly affords ample opportunity for migrations
of these and other cells. Of course, the actual migration of such cells has not
yet been shown, but that does not make the theory invalid.

These facts and theories are brought to the reader's attention at such length
because the doctrine of metaplasia has been over emphasized in attempts to
explain the peculiarities of tumors, and a feeling is abroad that tissues are far
more transmutable than positive evidence shows.

It would seem better to conceive a tumor of mixed histological structure to
arise from a mixed primordium, than to suppose its various component tissues to
be produced from the same primordium through metaplasia of its cells. And it
certainly seems more logical to suppose that heterologous tumors arise from
heterologous primordia of embryonal derivation, than from a normal tissue
primordium through anaplasia and metaplasia.

But whatever the tumor primordium, and whatever the cause of its growth,
continued enlargement is conditioned upon adequate nutrition.

It seems to be generally true that tissue growth precedes the formation of
the blood-vessels that supply it. For example, many invertebrate animals
attain to considerable size without distinct vessels of any kind, and among verte-
brates, the growing tadpole's tail increases in advance of the vessels that later
enter it. When it is stated, therefore, that growth is conditioned upon nutri-
tion, it does not necessarily refer to the presence of vessels.

There being a necessary balance between nutrition and growth, it was thought
and taught by Virchow that tumor growth resulted from excessive nutrition.
This seems unlikely as there is no reason to suppose that the cells act passively
in regard to the amount of nutrition they receive. They utilize only as much
of what is brought to them as their needs require. It may, therefore be supposed
that as the growing cells of the tumor require additional nutrition, means are
provided for supplying it.

In this respect the tissue of the tumor does not differ from normal tissue, or from that engaged in repair and regeneration.

Into the organizing thrombus new blood-vessels extend as needed; into granulation tissue new blood-vessels grow, and into the enlarging tumor they similarly grow. The size and number correspond with the need. How the proportion is regulated or determined is not known, but as the increasing size of the tumor increases its nutritive requirements, its vessels increase correspondingly, until should it become very large, its vessels may be immense. Into a large chondroma of the shoulder girdle, weighing 45 pounds, there entered an anomalous arterial trunk almost as large as the axillary artery. It had not pre-existed, but was newly formed. Whatever the nature of the tumor primordium, the vessels by which its later developed tumor mass is nourished, are always derived from the pre-existing adjacent vessels by budding and extension. The rapidity with which they are formed is in proportion to the rapidity of the growth of the tumor. If it grows rapidly and is composed of undifferentiated cells, its vessels may be obliged to develop more rapidly than they can be perfected. Hence, purely cellular tumors usually have imperfectly formed vessels, and the more hastily they are obliged to form, the more imperfect they will be. On the other hand, if the tumors consist of an adult tissue whose differentiation is slow, and whose increase in size is correspondingly slow, the vessels have plenty of time to attain to perfect development and may perfectly correspond with the normal type of structure. Again, it must be considered that a fully differentiated tissue of adult type, growing slowly and differentiating as it grows, will require but little nourishment as compared with a rapidly vegetating purely cellular tissue.

The new vessels begin as simple angioblastic endothelial off-shoots from the capillaries, but as they grow the connective tissue and muscle cells follow and provide for the media and adventitia. A certain amount of perivascular connective tissue also usually follows the vessels, so that most tumors become provided with a more or less regular fibro-vascular framework.

At first, the vessels are capillary but as they increase in size, they differentiate into efferent and afferent channels, i.e., arteries and veins, though the histological differences between the two are not so distinct as in the normal tissues and organs. The lymphatics of tumors may be assumed to arise through lymphangioblastic buds along the lines followed by the new blood-vessels. In the development of the embryo, the appearance of blood-vessels precedes that of the lymphatics by a considerable length of time, and in tumors they may be supposed to do the same. Where the blood-vessels are rapidly forming and imperfect, as in sarcoma, no lymphatics can be found.

The nerves of tumors are usually few, and imperfect, commonly lacking the myelin sheath.

The entrance of the vessels and nerves is not affected by the structural isolation or encapsulation of the tumor. Encapsulated embryomas, heterochthonous and independent in every particular, have blood-vessels like those of other tumors, derived from those antecedent in the nidus of the tumor.

When a tumor develops from a single primordium, it is said to be *unicentric;* if from several primordia, as shown by several simultaneously or successively

occurring lesions, *multicentric*. In multicentric tumors, however, care must be taken to determine that the first appearing tumor is not the parent of the others.

Tumors that arise independently of antecedent tumor growth are known as *primary tumors*. Multiple primary tumors sometimes occur, and may be of the same kind, or of different kinds.

Primary tumors sometime distributes their cells to nearby or remote parts of the body where they colonize and form daughter tumors, or as they are better known, *secondary tumors*.

Multiple primary tumors may be of different kinds multiple secondary tumors are except in most rare instances of the same kind. When great numbers of primary tumors occur simultaneously or successively, as in neuro-fibroma molluscum, or von Recklinghausen's disease, a suspicion is aroused that the condition is not a tumor, but either an infectious disease, or some kind of constitutional disturbance characterized by tumor-like lesions.

If the tumor primordium be of a slowly growing regularly differentiating character, resulting in the formation of some adult tissue, its increase in size is usually attended by compression of the surrounding more delicate tissues, whose parenchyma undergo pressure atrophy, while the more resisting framework becomes spread over the surface of the tumor as a *capsule* or rind that continually thickens on the outer surface through the addition of new substance, while thinned on the inner surface through the distending effect caused by the increase in the size of the tumor. Thus almost from the beginning of its formation a tumor may become more or less sharply separated from the tissues of its nidus. The capsule is not ordinarily or primarily a part of the tumor, and if the proper kind of an incision be made, the tumor may often be lifted out of its bed, leaving the capsule behind. But sometimes the tissues of the tumor becomes more or less blended with the capsule, *adherent capsule*, so that it cannot be done. In embryomas and teratomas, the capsule is a definite component of the tumor, and enucleates with it. But in such cases it is supplemented by the nidus capsule just described.

In proportion as the tissues of the tumor grow rapidly, and are unaccompanied by differentiation, and above all as the purely cellular types are reached, encapsulation gives place to circumscription, and that to lack of definite boundary and infiltration of the surrounding structures.

A tumor may be very well circumscribed, yet unencapsulated.

When cells in all parts of a tumor multiply with fair uniformity, it is said to grow by *interstitial expansion*.

When a tumor is composed of cells that multiply rapidly, and undergo no differentiation, the periphery does not abut sharply against the surrounding tissue, but advances against it in the form of a narrow fringe, composed of the tumor cells that are forced into the adjacent crevices until the elements of the invaded structure atrophy and make space for their better accommodation. The tissue is not so much pushed aside as invaded, and no capsule forms. Invasion progresses more rapidly where there is little resistance to the advancing cells, more slowly where there is more. If the quality of some of the invaded tissue is such that the cells cannot advance, it may be compressed and a partial

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capsule formed at that point, though the cells are invading and destroying else-where. Such marginal invasive growth is described as *peripheral infiltration*. Other parts of the same tumor grow by the usual interstitial expansion.

The circumscription of tumors with outlying cell fringes depends upon the length of the fringes, and this upon the disposition of certain cells rapidly to advance into such spaces as are available and appropriate. Carcinoma is characterized by the great length of its cellular fringes, and therefore by exten-sive and almost unlimited invasion. It tends to grow into and extend along the lymphatic spaces and vessels for long distances. As the result of interstitial expansion of the fringes, outlying portions of the tumor sometimes become more important and more bulky than the original growth. Wide-spread continuous growth of this kind, in carcinoma, has been described as *permeation* by Handley, and is thought by him, to be the chief means through which its secondaries originate.

Secondary cancers may, therefore, arise through the continuous growth of fringes at the ends of which nodular accumulations repeat the original structure of the tumor, but secondary sarcomas cannot be thus explained because of the restricted length of their fringes. Some other explanation must be sought for to explain their distribution, and is found in what is described as *metastasis*, or the transportation of the cells by currents of blood or lymph.

To understand metastasis it will be necessary to consider sarcoma and carci-noma separately.

Sarcomas consist of cells that multiply without transformation or differentia-tion, form great cellular accumulations, and are nourished by newly formed blood-vessels whose walls have not time to become perfectly formed. An examination of the most simple of these tumors shows the vessels to consist of nothing but endothelium, and in a few cases even that may be lacking, so that the blood circulates in unprotected spaces or sinuses between the cells of the tumor.

Under such circumstances it is easy to imagine occasional, cells of the tumor, loosened by the passing fluid, and swept into the venous circulation, being carried to the lungs or liver, according to the direction of the venous circulation, to be caught in the capillaries, where they may be destroyed, or proceed to multiply with the formation of secondary tumors.

Sarcoma growth is not infrequently attended by invasion of the walls of veins, which may be penetrated by the tumor cells with subsequent embolism.

In carcinomas, whose cells lack cohesiveness and extend along the lymph spaces and vessels, it is easy to imagine that cells singly or in groups, may be swept with the currents of lymph to the regional lymph-nodes where the first secondary tumors always appear. With the growth of each secondary tumor, the same process being repeated, the time at length comes, when, all of the lymph-nodes having been passed, the cells are admitted to the venous blood and transported to the lungs or liver where later secondaries are formed.

In those tumors whose cells undergo differentiation into fibrillar tissue, cartilage, bone, etc., there is no opportunity for transportation, and the tumors remain local. Most of the tumors whose cells are capable of transportation fall

into the group clinically known as *malignant*, those whose cells remain fixed, into that called *benign*.

Malignancy depends upon the structure of the tumor, the mode by which it grows, and the readiness with which its cells may be transported. These three factors confer upon the tumor *an inherent tendency to primary local destruction of the tissue by invasion, unlimited power of secondary colonization by permeation or metastasis, and the eventual destruction of vital organs*—supposing that some accident incidental to tumor growth does not supervene.

From this interpretation, it does not seem correct to include among the malignant tumors those whose injurious effect, even though it may result in the death of the patient, is the accidental outcome of their size or position.

For example, should a pedunculated tumor of the larynx become caught between the vocal cords, so that the patient is smothered to death, that would simply be an accident arising from the position of the tumor. Should a bony tumor grow upon the inner table of the skull and cause fatal cerebral compression, it would also be a mere accident of position: if the same tumor had grown upon the outer table of the skull, no harm would have resulted. If an enormous fatty tumor become so heavy that the patient can no longer move about, and divert so much blood that the patient is starved to death, it is but the accident resulting from the size to which the tumor attained.

The difference between such occasional accidental injury and the inevitable progressive destruction effected by a truly malignant tumor should be carefully kept in mind.

There are however different degrees of malignancy, corresponding to the particular methods of growth among those tumors characterized by invasive and distributive tendency. The most destructive may kill the patient in from six weeks to six months from the time of first observation; others may last for twenty or more years.

Tumor tissues are prone to retrogressive change. Mucoid degeneration rare in normal tissue, is common in tumors. Hyaline degeneration, extensive necroses and various forms of calcification, are also frequent. Some of these may depend upon peculiarities of the primordium, but most of them can be more easily accounted for. Thus, most tumors, sooner or later become subjected to traumatic injury. They are mechanically compressed, contused, and lacerated, or chemically mascerated in digestive and enzymic juices. They also frequently become infected.

Under these circumstances the softer cellular structures are crushed, the individual cells dislocated and distributed, and the delicate vascular structures lacerated so that blood is permitted to mix with the cells of the tumor. Larger vessels may become thrombosed and obstructed, the cells in their distribution suffering malnutrition and necrosis which, when superficial result in more or less extensive ulcerations and pave the way for later infections that always increase the local destruction, and may end in general and fatal infection. Or, should the necrotic areas include the larger blood vessels, they may open and extensive and even fatal hemorrhage occur. There are, therefore, many ways by which the patient suffering from a malignant tumor may be destroyed.

A manifestation of malignancy not yet touched upon is *recurrence* after surgical removal. Many tumors "come back," sometimes once, sometimes many times.

As far as knowledge goes, at present, it seems safe to say that if a tumor be completely removed, it cannot and will not come back. Yet the experience of the surgeon goes to show that no matter how thoroughly his operation be performed, tumors of certain kinds recur in a discouraging percentage of cases.

It must be clear that if any portion of the original tumor be left behind, it may go right on growing, and within a relatively short time after the operation show itself at the original location as a recurrence; that should any of the fringes of the tumor remain, it is equivalent to leaving some of the original tumor; that, if permeating filaments have extended into the adjacent structures, recurrence from them, though it take place at a distance from the original seat of disturbance is no more than continued growth of the original tumor; that if during the operation some of the tumor cells be scattered over the wound, recurrence taking place from their growth, would still be but a new appearance of the original tumor. Finally, that if before the operation, metastasis to the regional lymph nodes or to the viscera had taken place the tumor might reappear in them. The entire history of the primary, recurrent and secondary growths, is therefore, of one tumor substance, localized or distributed.

The recurrences have a histological structure that corresponds more or less perfectly with that of the original tumor. Occasionally the supposed recurrence shows a histological structure different from the original tumor, which is suggestive of origin from a different primordium, though usually attributed to a change in the type of the tumor through anaplasia or metaplasia.

In rare cases, the new tumor appears to develop from a new but adjacent primordium. Investigation has shown that cancers of the breast do not always grow from a single center, but sometimes from several in the same organ, or from several in both organs. Such multiple primordia may develop simultaneously or successively. In the first case appearing as multiple occurrences, in the second as recurrences or metastases.

Some tumors seem to change their type of structure and behavior from benign to malignant.

For example, the mixed tumor of the parotid, and the branchioma are encapsulated and benign tumors during their first years, and, if removed during that time, do not recur. Later they become invasive, and, if removed, persistently recur. Apparently the primordium in such cases is complex; descendents of one portion grow in youth, of the other later in life; both parts were there from the beginning.

One's opinion upon this matter will, no doubt, be influenced by his general conception of the tumor primordium. If he believe it to be normal tissue cells aroused to abnormal proliferative activity, it will seem simple, and he will probably incline to the supposition that metaplasia brings about the transformations; if he believe it to be composed of sequestered residual embryonal cells, it will appear complex and possessed of various latent capabilities, according as its different elements respond to the unknown tumor stimuli.

The cells of metastatic tumors vary greatly in the ease with which they colonize in the new environment. Many malignant sarcomas have no time to grow large; metastasis comes too soon and the secondaries are so numerous that vital organs are destroyed too early. Some require a long time to get a preliminary foot-hold, but once established, may grow rapidly. Some tumor cells distributed through the blood, develop in unexpected places, or only after and unusual length of time. Thus, the pigmented sarcoma of the eye, developing from the choroid, grows slowly, and is usually detected when quite small. As it is known to be a very deadly and dangerous tumor, it is usual to enucleate the eye as soon as it is discovered. The primary tumor may be no larger than a pea, and enclosed within the eye, whose globe is perfect. The entire tumor seems to be removed, and no recurrence takes place, but at any time, even as long as twenty years afterward, the patient may die from the same kind of pigmented tumors now situated in the liver.

In these cases there is no question of multiple primordia; it is one of metastasis. The cells carried to various parts of the body by the blood, died out except in the liver where for twenty years they have gradually become accustomed to the new surroundings.

Those who see in the tardy development of tumors an argument against the theory of development from embryonal residual material, will do well to consider the many years that these pigmented tumor cells may remain latent until some favoring condition excites them to active growth or makes such growth possible.

As metastasis is but the growth of tumor material transplanted to a new environment, it is not surprising that certain tumor tissues should prove to be experimentally transplantable. All that is needed is that the new environment shall be as good as the old. For generations experiments in tumor transplantation were made without attention to this detail, and a succession of failures lead many to believe the transplantability of tumors impossible. But the error was very simple; the early experiments were made by implanting human tumor tissues into the lower animals. So soon as Hanau successfully transplanted rat carcinoma into rats; and Moreau, Loeb, Jensen and others, mice tumors into mice, the mystery was solved. Homologous transplantation commonly succeeds heterologous transplantation usually fails. A great deal of experimental tumor transplantation has been done but with very little important addition to the knowledge of tumors.

The cultivation of tissue *in vitro*, begun by Ross Harrison, and greatly amplified by Carrel and Burroughs, was soon applied to the study of tumors, and has been industriously pursued by many investigators. In general it may be said that tumor tissue behaves more like embryonal than like adult tissue.

CLASSIFICATION OF TUMORS

In the present uncertain state of knowledge regarding tumors, no classification can be regarded as satisfactory, but to us the best seems to be that devised by Adami.

I. *Teratomata.*

Tumors derived from cells capable of giving rise to all of the tissues of the individual (totipotential cells).

A. Twin Teratoma (geminal or heterochthonous).

Example, Fetal inclusion.

B. Filial Teratoma (autochthonous), due to the segregation and subsequent growth of totipotential cells of the individual.

1. From non-germinal blastomeres.

Example Epignathus, congenital sacral teratoma.

2. From germinal cells.

(*a*) From aberrant germinal blastomeres.

Example. Sporadic teratoma of the cranium, etc.

(*b*) From unreduced ovarian and testicular germ cells.

Example. Ovarian and testicular teratomas.

Members of this class may be—

i. Complete, exhibiting derivatives of all three germ layers, or

ii. Incomplete, one germ layer failing to develop.

They may also be—

* Typical.

** Atypical.

II. *Teratoblastomata.*

Tumors (autochthonous) derived from pluripotential cells of the individual: Mixed tumors.

1. Diphyllic, containing derivatives of two germinal layers.

Example. Certain parotid and renal mixed tumors.

2. Monophyllic, containing derivatives from one germinal layer.

Example. Most renal mixed tumors.

III. *Blastomata.*

Tumors derived from unipotential cells.

1. Heterochthonous or teratogenic, the cells being derived from another individual.

Example. Destructive placental mole and chorioepithelioma malignum; epithelioma derived from an ovarian dermoid.

2. Autochthonous, from the independent growth of unipotential cells of the host individual.

Examples. All other tumors composed of cells of one order.

A. *Lepidic*, or Rind Tumors.

I. Lepidomas of the first order.

1. *Of Epiblastic Origin.*—Tumors whose characteristic constituents are overgrowths of tissues derived directly from the epiblastic lining membranes, or epiderm.

(*a*) Typical.—Papilloma, epidermal adenomata, (of sweat, salivary, sebaceous, and mammary glands, etc.).

(*b*) Atypical.—Squamous epithelioma, carcinoma of glands of epiblastic origin.

2. *Of Hypoblastic Origin.*

(*a*) Typical.—Adenoma and papilloma of the digestive and respiratory tracts, thyroid, pancreas, liver, bladder, etc.

(*b*) Atypical.—Carcinoma developing in the same organs and regions.

II. Lepidomas of the second order, or transitional lepidomas.

3. *Of Mesothelial Origin.* Tumors (mesothelioma) whose characteristic constituents are cells derived in direct descent, from the persistent mesothelium of the embryo.

(*a*) Typical.—Adenoma of the kidney, testicle, ovary, uro-genital ducts; adenoma of the uterus and prostate; adenomas originating from

the serous membranes, "mesothelioma" of the pleura, peritoneum, etc.

(b) Atypical.—Cancer of the above named organs; squamous endothelioma, so-called of serous surfaces; epithelioma of the vagina; adrenal mesotheliomas, hypernephroma.

4. *Endothelial Lepidomas.* Tumors originating from the endothelium of blood- and lymph vessels; lymphangioendothelioma; hemangioendothelioma, perithelioma, cylindroma, psammoma, cholesteatoma.

B. *Hylic*, or "Pulp" Tumors.

1. *Of Epiblastic Origin.*
Tumors whose characteristic constituents are over-growths of tissues derived from the embryonic pulp of epiblastic origin.
(a) Typical.—True neuroma; glioma.
(b) Atypical.—Glio-sarcoma.

2. Of hypoblastic origin.
Tumors derived similarly from embryonic pulp of hypoblastic origin. Chordoma.

3. *Of Mesenchymal Origin.*
A. Mesenchymal Hylomas.—Derived from tissues originating from the persistent mesoblastic pulp, or mesenchyme.
(a) Typical.—Fibroma
Lipoma
Chondroma
Osteoma
Myxoma
Leio-myoma
Angioma
Myeloma
(b) Atypical.—Sarcoma (derived from mesenchymatous tissues), with all of its various subdivisions—
Fibrosarcoma
Spindle celled sarcoma
Oat shaped celled sarcoma
Chondrosarcoma
Osteosarcoma
Myxosarcoma
Lymphosarcoma
Chloroma
Angiosarcoma
Melanosarcoma (origin debatable).
B. Mesothelial Hylomas.
Tumors which are overgrowths, similarly, of tissues derived from the embryonal pulp of definitely mesothelial origin.
Rhabdomyoma.

In marked contrast with this is the "listing" of tumors without classification, that has been suggested by Mallory, and which has some advantages from the practical point of view. In explaining his system, Mallory says

"A knowledge of the embryologic development and appearance of the normal tissues is important for two reasons. If a tumor grows rapidly, its cells do not have time to differentiate to any extent; they remain of an embryonic type which must be recognized (nerve cells and striated muscle cells, for example). Embryology is useful in explaining the occurrence of tumors in certain situations, for instance, a glioma of the nasal sinuses, or over the coccyx; adrenal cell tumors in the kidney and liver; a chordoma at the base of the skull; and epidermoid carcinoma deep in the neck and not connected with the skin. Under every recognized variety

of tumor there should be grouped both the slowly growing and rapidly growing tumors built up by the multiplication of the same type cell. In no other way is it possible fully to understand each variety of tumor and find out all its characteristics. The type cell is the one important element in every tumor. From it the tumor should be named, not from some peculiarity of minor importance, such as mode of growth or arrangement of cells, or form of retrograde change. There occur in the human body some fifteen different distinct varieties of cells, giving rise to tumors, which may be denominated type cells. Each of these fifteen type cells gives rise to a series of tumors which grow at various rates of speed. All gradations occur between the slowest and fastest growing. The list of type cells and of the tumors arising from them is as follows:"

Type Cell	Name of the Tumor
1. Fibroblast (connective tissue cell).	Fibroblastoma (fibroma, fibro-sarcoma).
2. Myxoblast (mucous connective tissue cell).	Myxoblastoma (myxoma, myxo-sarcoma).
3. Chondroblast (cartilage cell).	Chondroblastoma (chondroma, chondro-sarcoma).
4. Osteoblast (bone cell).	Osteoblastoma (osteoma, osteo-sarcoma).
5. Lipoblast (fat cell).	Lipoblastoma (lipoma).
6. Leiomyoblast (smooth muscle cell).	Leiomyoblastoma leiomyoma, l e i o m y o-sarcoma).
7. Endothelioblast.	Endothelioblastoma.
(a) Blood-vessel endothelium.	Hemangioendothelioblastoma, (hemangioma, angioma).
(b) Lymph-vessel endothelium.	Lymphangioendothelioblastoma (lymphangioma).
(c) Dural endothelium.	Dural endothelioblastoma (dural endothelioma).
8. Lymphoblast (lymphocyte).	Lymphoblastoma (lymphosarcoma, malignant lymphoma, lymphatic leukemia).
9. Myeloblast (myelocyte).	Myeloblastoma (myelogenous leukemia; chloroma).
10.	..........................(Myeloma).
11. Melanoblast (pigment cell).	Melanoblastoma (melanotic s a r c o m a; melanoma).
12. Rhabdomyoblast (striped muscle cell).	Rhabdomyoblastoma (rhabdomyoma, rhab-·domyosarcoma).
13. Glioblast (neuroglia cell).	Glioblastoma (glioma, gliosarcoma).
14. Neuroblast (nerve cell).	Neuroblastoma (neuroma).
15. Epithelioblast (epithelial cell).	Epithelioblastoma (adenoma; papilloma; carcinoma).

"Besides the fifteen varieties of simple tumors, there are other tumors due to the proliferation of cells of an earlier embryonic type, which are capable of differentiation into two or more simple adult type cells. These tumors are called mixed tumors. Several varieties occur, some very simple, others more complex in structure. The most complex tumors arise from cells capable of development into a fetus."

THE SIMPLE BLASTOMAS

FIBROMA

A fibroma is a tumor composed of fully formed fibrillar connective tissue. It is treated in most text-books as though it was one of the most common, most simple, and most easily understood of the tumors. All this is wrong. It is not common, it is not simple, and it is not easy either to recognize, or to under-

stand. It becomes confused with inflammatory new formations on the one hand, and with sarcoma on the other. It is by no means certain that the different growths called by the name have much in common.

The following tabulation attempts to show the relationship of these different lesions:—

I. *Fibromatoids.*
    A. Diffuse connective tissue hyperplasias.
       Cicatrix.
       Elephantiasis.
    B. Circumscribed but not encapsulated connective tissue growths of tumor-like appearance.
       Keloid.
       Painful subcutaneous tubercle.
       Polypi.
          1. Sub-cutaneous—Neuro-fibroma molluscum.
                           Dermatolysis.
          2. Sub-mucous— Nasal polypi.
                         Laryngeal polypi.
                         Uterine polypi.
       Fibrous Epulis.
II. *Fibroma.*
    Circumscribed and encapsulated.
    A. Simple Fibroma.
       Fibroma durum or desmoid.
         Ovarian fibroma.
         Uterine fibroma.
    B. Composit Fibroma.
       Fibro-adenoma.
       Periductal fibroma.

Cicatrices and chronic inflammatory connective tissue formations lead insensibly into fibroma, and confusion has thereby resulted. Nothing should be regarded as a tumor, unless it conform to the requirements of tumor as defined in the preceding section. Many cicatrices are local and fairly well circumscribed. An example that came under the writer's observation some years ago from the clinic of the late Prof. John Ashhurst, was a lesion upon the thenar eminence of the hand of a machinist, that had been removed as a fibroma. It was about the size of a hen's egg, well circumscribed, though not encapsulated, densely fibrillar and solid. The patient had some years before injured the hand, and asserted that a fragment of a screw had remained in it. When the mass was cut through, a small cavity was found, and in it was a fragment of steel. The growth was not a tumor, but only a great hyperplasia of connective tissue resulting from the chronic irritation effected by the foreign body.

The immense, and usually diffused connective tissue enlargements of elephantiasis, have already been referred to as being classed as tumors by some writers. It is a mistake: whether the tissue proliferation be caused by filarial worms in the lymphatics, previous streptococcic or other micro-organismal infection, or the bite of a rattle-snake, the recognized nature of the irritant and the diffused form of the lesions are sufficient to exclude them from the tumor class.

The peculiar more circumscribed new formations known as the *keloids* should probably be treated in the same manner. They occur in seemingly predisposed individuals after injuries accompanied by breach in the continuity of the skin, and were first described by a French writer named Alibert, who named them from the Greek κηλὴ, a claw. The wood now appears in the literature with two spellings, Keloid and Cheloid.

Alibert recognized two varieties:

1. True or spontaneous keloids that arise without explanation.

2. False keloids that result from excessive cicatrization after traumatic injury, and are what are ordinarily meant when keloids are mentioned. But in addition to these there appears, in the literature, another lesion, the keloid of Addison, which is entirely different, and now known to dermatologists as "morphea."

The keloid of Alibert, is a mass of cicatricial fibro-connective tissue arising spontaneously or in a cicatrix, and composed of coarse hyalinized collagen fibres, for the most part running parallel, and without elastica. The

FIG. 144.—Enormous keloids of the neck. (*Duhring.*)

periphery fades into the surrounding connective tissue without capsule or distinct limits. In Caucasians the lesion is usually of a pinkish red color; in negroes, a little darker than the normal skin. The spontaneous keloids probably depend upon minute lesions to which no attention was paid at the time of first injury. The growth is slow and persistent for a long time, sometimes for many years, then ceases, and after a longer or shorter time commonly retrogresses, and may disappear, leaving only a normal scar. The occurrence following injury, the lack of circumscription, and the tendency to eventual disappearance are all opposed to the identification of the lesion with the tumors.

Neuro-fibroma molluscum or *von Recklinghausen's disease* is characterized by the multiple occurrence of small and large somewhat soft, imbedded and pedunclated nodules that project from the skin. There may be hundreds of them, and though they usually vary from a pea to a walnut in size, some may be as large as cocoanuts. The scalp is frequently affected, but in a slightly different manner, its skin becoming loose, and with a great quantity of subcutaneous tissue, hanging in folds that sometimes reach to the shoulders. In case the latter condition occurs alone, it is known as *dermatolysis*, and is sometimes confused with elephantiasis. Neuro-fibroma molluscum is certainly much like tumor in appearance, but the lesions are commonly preceded by periods of reddening and pigmentation of the skin, they are associated with enlargement of the adrenals and hypophysis cerebri, and the disease is markedly hereditary.

Further when the lesions are examined histologically, they are found to consist of skin beneath which are masses of fibrillar tissue not in any way separated from the subcutaneous connective tissue of which they seem to be a part, and more or less definitely in relation with nerve fibrils, some of which are degenerated. It seems probable, therefore, that some constitutional disturbance is responsible for the local tumor-like manifestations. Nor does the frequent occurrence of deeper nodules in association with those in the skin exclude this idea. The latter are usually in association with the nerves, the relation of superficial to deep lesions being not unlike that occurring in nodular and nervous leprosy.

FIG. 145.—Keloid of face following a burn. (*Mallory,* *"Principles of Pathologic Histology."*)

FIG. 146. — Neuro-fibroma molluscum or Von Recklinghausen's disease. (*Weidman.*)

In nearly all books the nasal polyp is classed as a tumor, formerly as a myxoma, more recently as an edematous fibroma. But the relation of nasal polypi to chronic inflammatory disease of the nose is well known and openly stated, and as polypi occur upon other mucous membranes as a result of chronic inflammation, it is possible that they should be excluded from the class of true tumors. Moreover, when the nasal polypi are examined microscopically, they are found to be composed of sub-mucous tissue, that cannot be differentiated from hyperplasia. If one be removed, others may arise, without any necessary connection with the original one. In rare cases only does the polyp consist of tissue that
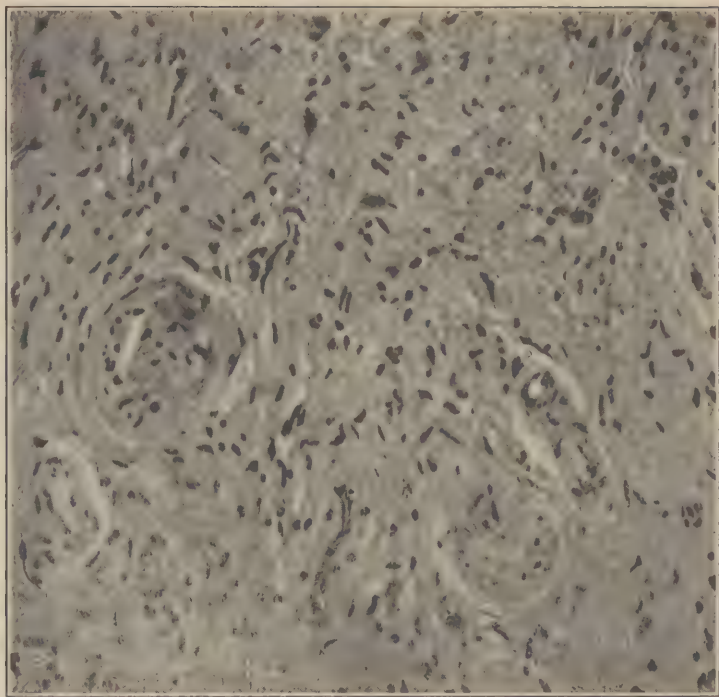
FIG. 147.—Microscopic section of one of the small tumors from a case of neuro-fibroma molluscum. (*Photomicrograph by Dr. F. D. Weidman.*)

FIG. 148.—View of the right nasal fossa, showing numerous polypi growing from the middle of the turbinated bone. (*Bowlby and Andrewes.*)

can definitely be shown to have arisen from a residue of the original polyp. The more definitely the tumor is pedunculated, the more distinctly like a tumor it appears.

But this requirement of circumscription must not be too much dwelt upon. Some lesions not definitely circumscribed may be true tumors, as the *fibrous epulis*. This is a nodular mass of fibrous tissue that springs from the gums,

FIG. 149.—Multiple neuromata of the peripheral nerves. *A*, Nerves of the right arm; *B*, the left sciatic with its branches; *C*, the left anterior crural with its branches. (*Prudden's case.*) (*Ewing.*)

especially about carious teeth, is convered with mucous membrane, attains to a size as great as a walnut in some cases, and is not at any point separated, by a capsule, from the adjacent connective tissue. As, however, this is only one of a number of epuli, the others being composed of spindle cells, or spindle and giant cells and classified as sarcomas, and still others of epithelial tissue and classified as carcinomas, there seems to be little room for doubt about the propriety of considering the fibrous epulis a tumor.

There can be no doubt, however, about the true tumor nature of fibrillar tissue growths, when their substance is enclosed within a capsule.

Some of these occur upon the nerves, where they form more or less rounded, nodular circumscribed, and almost completely encapsulated single or multiple

tumors, varying in size from a millet seed to an orange. They are soft, and sometimes more or less mucilaginous in consistence, translucent in appearance, and upon them the nerve fibres are spread out like a tape, only occasionally penetrating into their substance. They are known as *false neuromas*.

These tumors spring from the endoneurium and perineurium, and are composed of fibrillar connective tissue which is sometimes pervaded with soft mucinoid substance, giving the impression that the tumor is really myxoma—as, indeed, it may be. The nerves suffer atrophy from the stretching and compression, so that palsy may result from their presence.

Nearer the periphery, but still upon the nerves small hard connective tissue tumors sometimes occur. They seem to be single, and press upon the nerves causing pain of dull aching character when undisturbed, and acute pain like an electric shock when pressed upon. These have been called "*painful subcutaneous tubercle*" by Sutton. They are always small, most of them not larger than grains of rice, a few as large as peas. They are not so sharply circumscribed as the false neuromas described above, nor so definitely encapsulated. The structure consists of delicate but closely approximated connective tissue fibrils, through which nerve fibres pass.

The most perfectly encapsulated fibromas probably occur in the ovary. They grow quite large, are completely surrounded by a thin capsule, and are firm and heavy.

Many of the older books speak of fibromas of the uterus, but what is usually meant is the "*fibroid*" which is in almost all cases a mixture of unstriated muscle and fibrillar connective tissues, and therefore, more correctly a fibromyoma. Pure fibromas of the uterus are not common.

But lack of circumscription is not the only diagnostic difficulty to be overcome in the study of fibroma. Microscopically these tumors consist of fibrillar connective tissue, but its exact state as regards differentiation is variable, as is shown by the number of cells that it contains. Long ago it was pointed out that some of these tumors recurred, and English pathologists called them "*recurrent fibroids*." Such tumors resemble spindle-celled sarcoma. Does cellular structure in fibroma connect it with sarcoma? Is the increase in the number of cells an indication that the tumor is growing or an evidence of anaplasia tending towards malignant behavior? How many cells may a fibrillar connective tissue tumor have and still be fibroma? How many must it have to be called sarcoma? These are questions that cannot be satisfactorily answered at present. In many simple fibromatoid conditions an excessive number of cells may indicate no more than that the connective tissue is in rapid multiplication; in some of the fibromas it occurs locally, and may simply indicate that that particular part of the tumor is growing. Sometimes a tumor thought to be a fibroma recurs with a more cellular structure, and again with a purely cellular structure, sarcoma. Is it to be supposed that its nature had changed by metaplasia or anaplasia? If some other part of the original tumor had been examined, would more cellular parts have been found, and the diagnosis been more guarded. The microscope is not an infallible guide in determining the malignancy or benignancy of tumors of this class.

The cut surface of a fibroma presents an appearance characteristic of all tissues made up of elongated elements in parallel but not straight course. It is *fasciculated;* that is, slightly differentiated or mottled by the alternate longitudinal, oblique and transverse sections of the curling and intertwining bundles of the fibres and cells of which it is composed. The color is variable; some of the tumors are white some gray, some pinkish gray. Occasionally there are small or considerable deposits of calcium salts and, more rarely, of bone. It is not

FIG. 150.—Pedunculated fibroma of the chest wall. (*Jeffries and Maxwell.*)

uncommon to find areas of degeneration—hyaline, mucoid—in the older parts. Hemorrhages are rare, since the blood-vessels are perfectly formed. Those observed can usually be referred to traumatism.

The connective tissue is fibrillar, and may be coarse or fine. In the former case the tumor is usually fairly hard; in the latter soft. The greater number of fibres are of collagen, which may be of normal appearance, or be softened by the mucinoid change, or swollen by the hyaline change. Among them may be a comparatively small quantity of fibroglia and elastica. The cells are usually comparable to those of the normal adult connective tissue—that is, there are scarcely any distinct cells, but there are regularly scattered nuclei, squeezed between the fibres and bundles of fibres in whose formation they have partici-

pated.   As the tumors are usually growing, and as growth can only take place through the multiplication of cells, those parts that are actively vegetating must be more cellular than the inactive ones, and there may be found well contoured cells with vesicular nuclei, some of which may be in some stage of mitosis. Tendency to malignancy must not be deduced from this alone; it only indicates growth.   Some French pathologists lay great stress upon the occurrence of
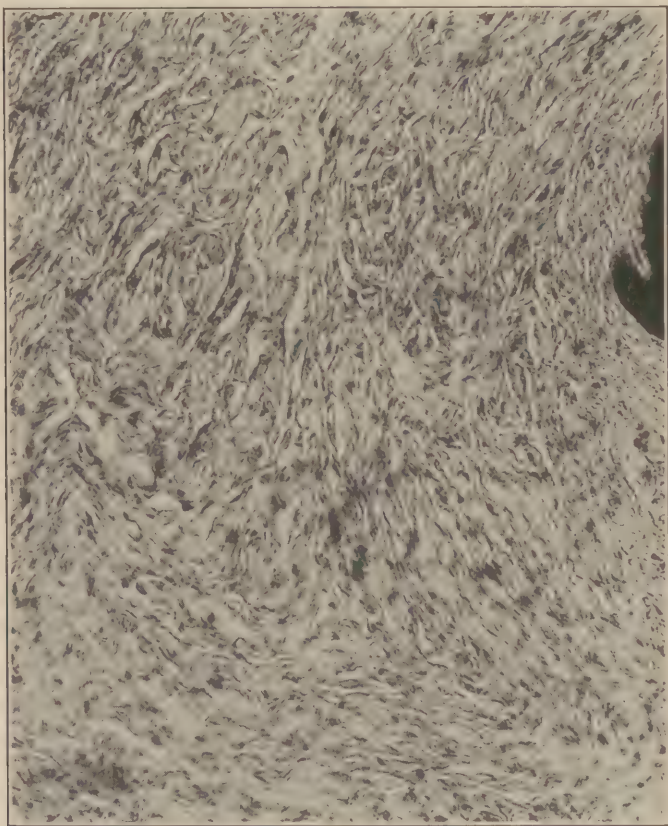
Fig. 151.—Microscopic section of a soft fibroma.   (*Photomicrograph by Dr. F. D. Weidman.*)

abnormal and over large nuclei and teach that if monstrous nuclei occur in excessively cellular areas with rapid mitosis, malignant disposition may be suspected.

Malignant disposition is first shown by recurrence, which is usually repeated several times before the increasingly cellular structure of spindle cell sarcoma is reached.   It is only when this stage is reached that metastasis need be feared.

But the possibility of malignancy may have been overemphasized: uncomplicated fibromas are benign, do not recur when excised, and never give metastasis.

MYXOMA

A myxoma is a tumor composed of mucous-forming connective tissue. Its characteristic cell, according to Mallory, is the myxoblast, and unless it is derived from such cells, and characterized by the continuous formation of connective tissue mucous, it should not be called myxoma. This is emphasized because not a few edematous fibromas, and mucous degenerated fibromas and sarcomas have been called myxomas and myxo-sarcomas. The formation of the mucus must be primary, and not secondary.

Fig. 152.—Myxo-fibroma of the wall of the intestine. (*From a specimen in the Pathological Museum of the University of Pennsylvania.*)

It is sometimes stated that the prototype of the mucoid tissue is to be found in the umbilical cord. As there is no mucus tissue in the normal adult body, that embryonal structure seems the best prototype, and it affords a fairly good illustration of the fact, once before pointed out, that the structure of a tumor rarely bears perfect correspondence with the normal tissues, for it must be very rarely indeed that the microscopic structure of myxoma corresponds with that of the jelly of Wharton.

A tumor whose structure corresponds with an embryonal tissue only, should be, and probably always is derived from embryonal cells, yet some regard it as the result of metaplasia.

Myxomas are comparatively rare tumors. In many laboratories, however, they do not seem to be so. The softness, moistness, and translucence of the tumor tissue when grossly examined, and the wide separation of the fibres and cells when sections are examined with the microscope, may give an erroneous impression, and edematous tissues are frequently called myxomatous. In all

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cases some specific stain such as mucicarmine or muc-hematine should be applied. The importance of this is shown by the fact that in many of the best laboratories, until a few years ago, sections of nasal polypi were shown to students as characteristic examples of myxomas; now they are known to be edematous fibromas.

As it was necessary to differentiate between fibromas and fibromatoids so it seems well to recognize the possibility of there being myxomas and myxomatoids. The true myxoma is a tumor, and is usually well circumscribed and sometimes
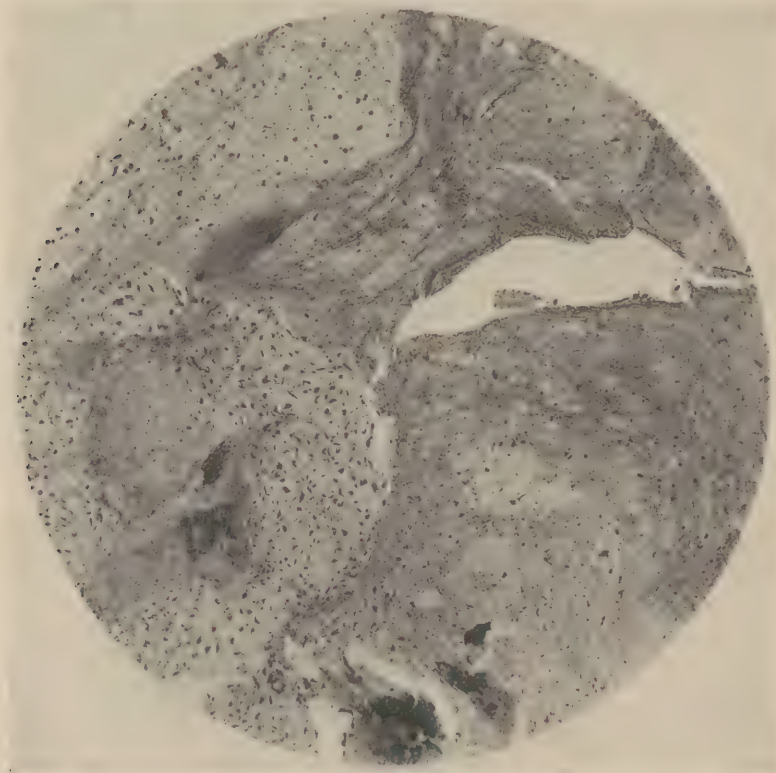
FIG. 153.—Microscopic section, showing a pure myxoma of bone, containing a few islets of osseous tissue, and the eosin-staining fibrous tissue that separates the myxomatous tissue into larger and smaller islands. (*Bloodgood*.)

encapsulated. It is soft, sometimes fluctuates, is translucent, moist, and when cut and pressed, permits a mucilaginous fluid to exude as from a sponge. The cut surface is usually gray or pinkish gray. Hemorrhages may cause parts of it to appear reddish.

When examined histologically, it is found to consist of a reticulum of cells of spindle and stellate shape, in the meshes of which the mucus collects uniformly. But the same perplexing variation in the number of cells in different areas that was discussed in the case of fibroma, is encountered, and the same difficulty in distinguishing between the harmless benign myxoma and the extremely danger-

ous and malignant myxo-sarcoma is found.   Tumors with excessive cellular areas should be regarded with suspicion.

But uncomplicated myxoma is a benign tumor for which no return, and certainly no metastasis need be feared.

Myxoma occurs in the sub-cutaneous, sub-mucous, sub-peritoneal, and neural connective tissues by preference, but may occur in the intermuscular septae, and in the fascia.   Rare small polypoid tumors of the left ventricle of the heart commonly show myxomatous structure.

CHONDROMA

A chrondroma is a tumor composed of cartilaginous tissue.

In the section upon "Mixed Tumors" in the first part of this book, certain tumors in which cartilage is present as an important or even diagnostic component, were described and explained, but they were not chondromas.

Before entering upon the detailed consideration of the subject, it may be well to tabulate the new growths of cartilage, and see how they are related to one another.

I. *Chondromatoids.*
   1. Ecchondroses.   These are cartilaginous outgrowths from the edges of the articular cartilages, passing through the capsular ligaments.   They are commonly multiple and small.   They seem to result from chronic irritation, and are common in rickets.
   2. "Joint mice" and "rice bodies" are intra-articular cartilaginous formations varying in size, according to the size of the joint, from rice grains to hazel nuts.   They are formed through chondrification of the villi of the synovial fringes, supposedly as the result of irritation.
II. *Chondroma.*
   1. Enchondroma.   These usually arise from vestiges of embryonal cartilage retained at the junctions of the shafts and epiphyses of the long bones, or about the ribs, scapula or pelvis.   They may grow from the endosteum and occur singly or multiply in the medullary cavity.
   2. Ecchondroma.   These are bony outgrowths from pre-existing cartilage and occur in the larynx, in the trachea, or from the costal cartilages.
   3. Osteoid Chondroma.   This tumor grows from the periosteum of the long bones, and is a peculiarly mixed structure consisting first of dense fibrillar tissue of the periosteum, which becomes first chondrified, then penetrated by trabecula of ossein, and later tends to ossification.
   4. Chondroma Myxomatodes.   A chondroma with myxomatous change.
III. *Chordoma.*   This tumor described in the section upon the Congenital Conditions of Surgical Interest, was first named by H. Müller Ecchondrosis physalifora.

. Cartilage seems to be a product of specialized connective tissue cells, or chondroblasts, which Mallory declares to be fibroblasts that have especially acquired that function.   According to his view, the chief difference between cartilage and fibrillar tissue is the separation of the fibrillae of the latter by chondrin.   The fundamental structure is fibroblasts with their fibrils of collagen, fibroglia and elastica.   The cartilage is fibrous if collagen preponderates, elastic if elastica preponderate, and hyaline only when the chondrin is present in such large quantities as to separate the fibrillae widely, and enclose

the cells, in groups, in small spaces in the homogeneous appearing matrix.   This conception of the structure and formation of cartilage, enables one to understand how it grows and why it varies, as well as to realize that there is no reason why its different varieties may not at times occur together.

New cartilage is probably never formed from the cartilage cells of the lacunae. They have completed their function and are at rest, if not degenerating; it is

Fig. 154.—Chondroma of the humerus and shoulder girdle weighing 45 pounds.   (*Dr. J. Ben Johnson.*)

always the result of cells at the periphery which are more of the fibroblastic type of appearance.   It is not known whether cells of this kind are always present at the surface of the bones, but so soon as a bone is fractured, they make their appearance from some source to provide the provisional callus and assist in the repair.   It is well known, and has frequently been demonstrated, that bits of embryonal cartilage remain in the substance of bones whose growth has depended upon the presence of epiphyseal cartilage. From such vestiges tumors may later grow.

Chondromas nearly always form rounded nodular tumors with great density and moderate elasticity, in relation with bone or cartilage.

When divided they are usually found to be surrounded by a dense rind of connective tissue which is often described as a capsule, but which, for the most part consists of the perichondrium from which the cartilage is growing, and only

FIG. 155.—Multiple chondromas of the phalanges and metacarpal bones. (*Meyerding.*)

in small part of the displaced and compressed connective tissue of the tissues into which it grows, and which constitutes the real capsule. In most cases the substance is divided into lobules more or less definitely separated from one

another by fibrous partitions which are vascular axes by which the growing cartilage is nourished.

When the structure is examined histologically, it is usually not simple at first glance. One of the larger nodes may be found to consist of typical hyaline cartilage, but as the center is left and the periphery approached, the lacunae become smaller and more numerous, and the tissue more and more fibrous until the cellulo-fibrous layer of the perichondrium is reached. But another neighboring node may show no such gradual transformation, its typical and adult hyaline cartilaginous structure, abutting upon the perichondrium as in a section of normal costal cartilage. This probably means that in the former node the cartilage was forming, and in the latter temporarily, at least, finished.

But in addition to this are differences having to do with rapidity of growth, type of cartilage formed, and the duration of the lesion, and perhaps also depending upon the state of nutrition of the cartilage formed, or having some relation to the primordium of the tumor. Attention ought to be paid to these factors as they have some bearing upon the disposition of the tumor.

The largest chondroma that has come under the writer's examination was a tumor that grew from the scapula and shoulder girdle, and weighed forty pounds. When examined microscopically, it was found to be chiefly composed of adult hyaline cartilage. The histological structure was typical; in a hyaline ground substance small collections of two, and four cells were enclosed in rounded spaces widely separated from one another.

More common is a structure resembling the embryonal hyaline cartilage that forms the model of the long bones, and in which single cells of spindle shape are uniformly distributed throughout the hyaline matrix, with only narrow intervals between them.

A third type of structure resembles fibro-cartilage, in which dense bands of connective tissue have occasional lacunae containing cells arranged much as in the intervertebral discs. This sometimes occurs between nodes of hyaline cartilage, and may escape detection because of the presence of the more striking and more easily recognized variety. In rare cases elastic cartilage may be present, but no case showing it distinctly has come under our observation.

The last variety is that in which there is admixture of mucoid tissue. Such cases are usually cellular, and pass into sarcoma both in structure and disposition. Bloodgood declares of such tumors that "the only ones cured were those in which the involved bone had been removed by resection or amputation without exposure of the tumor tissue."

As it is not uncommon for several varieties or appearances to occur in the same tumor, it will be understood that the histology of chondroma is not so simple as might be inferred from its definition.

There seems to be occasional difficulty in differentiating between periosteal chondroma and exostosis. Bloodgood points out that in the former the cartilage is centrally situated, while in the latter it forms a covering or capsule about the bony growth beneath.

The external or periosteal chondromas usually disturb the bone but little, though they may excavate a fossa in its surface, by atrophy. On the other

hand, the centrally situated ones destroy the bone by distending its shaft until it becomes a thin and brittle rind about the cartilage.

Centrally situated chondromas are apt to be multiple, especially when occurring in the phalangeal bones of the hands and feet, where they are fairly common. These cases frequently suffer from great deformity of the members which are rendered useless. Curiously enough, this form of multiple chondroma is distinctly hereditary.

Simple chondroma is a benign tumor, but is has peculiarities that require especial mention, as they place it on the border line between the benign and

Fig. 156.—Roentgenogram of a chondroma of the lower end of the femur. (*Meyerding.*)

malignant tumors. Thus, it is occasionally metastatic, even in cases that show no indication of suspicious character. The explanation is found in occasional erosion and penetration of the veins, by the growth, which then follows them for considerable distances—sometimes to the heart itself. Fragments broken from these venous extensions are supposed to be the source of the metastatic growths.

Mucoid degeneration is frequent in chondromas, and sometimes the tumor contains cysts filled with mucus. Calcification and ossification also occur. This is rather a characteristic of cartilage than of chondroma, as it is well known that as age increases there is a disposition for the laryngeal cartilages to ossify, and the calcification and ossification of the costal cartilages is common. The skin stretched over large chondromas may ulcerate, and the resulting infections become troublesome.

A rare tumor commonly confused with chondroma is the chordoma. Its structure bears some histological resemblance to cartilage, but has an entirely different embryogenesis. It is described and explained in the section upon Congenital Conditions of Surgical Importance.

OSTEOMA

An osteoma is a tumor composed of osseous tissue. As definite, separate, independent entities they are rare; most of them really should fall in the class of hyperplasias as is shown by the following classification:

A. *Osteomatoids*, or bony growths not to be classified as true tumors.
    I. Arising through hyperplasia of bone or bone-forming tissues.
        1. Enostoses—occuring inside of the bone.
        2. Exostoses—occurring on the outer side of the bone. They consist of bony tissue of varying density, may occur in connection with any bone, and frequently arise in consequence of old fractures, sinuses etc., and present various appearances, as follows:—
            (*a*) Ivory-like exostoses of the cranial bones.
            (*b*) Exostosis cartilaginea or ossifying ecchondrosis. This occurs at the ends of the long bones, or at the epiphyseal junctions, and is convered with cartilage upon which there is frequently a synovial bursa, which gives it the occasionally employed name, exostosis bursata.
            (*c*) Diffuse and localized bony enlargements such as characterize akromegaly, leontiasis ossea, etc.
        3. Hyperostosis. This is a general hypertrophy of a bone or the greater part of a bone, usually following arthritis, periostitis, or osteomyelitis.
    II. Arising independently of definite connection with bones or bone-forming tissues, either as the result of the dislocation of osteoblasts, or through metaplasia of other varieties of connective tissue. The origin is usually uncertain. They occur:—
        1. In the tendons.—ossification of the tendons is normal in some lower animals.
        2. In the muscles—in myositis ossificans.
        3. In the dura of the falx cerebri.
        4. In the penis. A few of the lower animals such as the walrus, and raccoon, normally possess penile bones.
        5. In the sclerotic and choroid of the eye, especially in phthisis bulbi.
        6. In the pulmonary trabeculae.
        7. In the valves of the heart, the aorta, and some of the smaller vessels.
        8. In cicatricial tissue and in fibromatoid growths.
B. *Osteoma*, a true tumor composed of osseous tissue,
    I. According to structure:
        (*a*) Osteoma eburneum, composed of an ivory like substance.
        (*b*) Osteoma durum, composed of dense bone.
        (*c*) Osteoma spongiosum, composed of cancellous bone, with abundant marrow cavities.
    II. According to seat of occurrence:
        (*a*) Homoplastic osteoma. These grow from pre-existing bone, and include,
            1. Osteoma centrale, or endosteal osteoma.
            2. Osteoma corticale, or periosteal osteoma.
C. *Dental Osteoma*, or tumors composed of dentine. They are rarely distinct and separate from the teeth, and are commonly known as Odontomas. They are fully described in the part of this work dealing with the Congenital Conditions of Surgical Interest.

When this arrangement is carefully reviewed, it will be found that there are in reality, very few distinct tumors composed of bone, though tumor-like enlargements and excrescences are common, and their structure varied.

The new bone is formed by osteoblasts some of which are scattered throughout most bones, but concentrated in great numbers in the periosteum and endosteum. On this account, most bony growths arise from one or the other of these membranes, though not necessarily, as the scattered osteoblasts may originate them. The latter origin seems to apply in the case of tumors arising in the cancellous substance of long boxes, and from the bones of the cranium and face. This is indicated by the absence in these cases of a periosteal membrane.

In some cases the new formation of bone is preceded by hyaline cartilage; in others it proceeds directly from the periosteum, in still others from the undiscovered scattered osteoblasts. In the first two it is surrounded
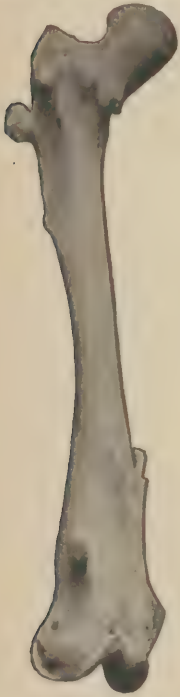
Fig. 157.—Femur with multiple exostoses. (*Aschoff*.)
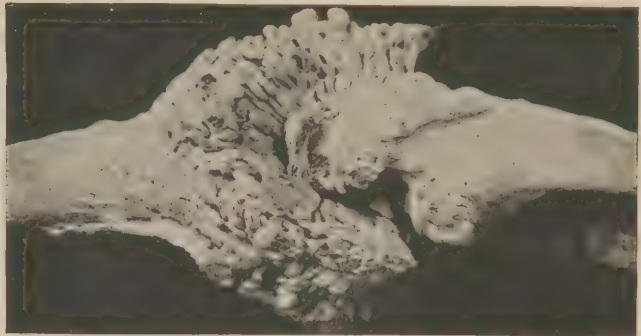
Fig. 158.—Exostoses of the elbow-joint. (*Stengel and Fox.*)

by a kind of dense capsule consisting of the periosteum or perichondrium; in the latter it has none. Different types of bony tissue may occur in the same morbid growth, but usually one type is pretty well adhered to.

The histological structure is usually unmistakable, though complete Haversian systems do not always appear; however, the lamina with the bone corpuscles in their lacunae, with communicating canaliculi show well.

Osteoblasts and fibroblasts belonging to the periosteum are usually abundant.

Bony tumors, as might be expected from the amount of differentiation required in their structure, grow very slowly. They may be attended by pain, caused by the displacement of tissues or by compression, but ordinarily this symptom is unimportant. The amount of damage done varies according to the position of the growth. Thus in the orbital cavity their development is soon shown by displacement of the globe of the eye; in the superior maxilla by the displacement of the teeth and trespass upon the mouth. In the inner table

of the skull they may cause compression of the brain; in the pelvis, compression and obstruction of the viscera.

On external portions of the skeleton they form rounded nodular dense hard masses with deformity and diminished mobility according to position.

Their origin can frequently be traced to vestiges of the embryonal cartilage from which the bone developed, but when the tumors attain to any considerable

FIG. 159.—Osteoma of orbit. (*After Knapp.*)

size this is impossible; and the only inkling of the origin is that indicated by the position in which the tumor develops.

As already said, the osteomas of the long bones occur chiefly as exostoses. and arise from the epiphyseal cartilage remnants. Of the tumors that arise from the facial and cranial bones and trespass upon the frontal sinuses, the orbital cavity, and the antrum of Highmore, and of which Le Grange collected 148 cases, some seemed to arise from the periosteum, others from cartilaginous vestiges of the ethmoid bone.

In the nasal and antral cavities bony tumors are sometimes found lying free i.e., without attachment to any other bone. They are sometimes called "dead osteomas" and are attributed to vestigial cartilage of the ethmoid bone.

The most frequent of the bony growths is the exostosis, arising from the vestigial epiphyseal cartilage. It may occur upon any bone of cartilaginous formation and is particularly common at the lower end of the femur, but may also occur on the ribs, clavicle, scapula, pelvic bones, and phalanges. It may be single or multiple, and may also be congenital, or acquired. The central part is composed of bone, upon which there is usually a layer of cartilage, and in

the case of the femoral tumors, a superimposed bursa supposedly derived from the synovial membrane of the neighboring joint.

Osteomas are benign tumors, and their diagnosis is usually easily made without the aid of the microscope, but the pathologist is frequently called upon for a prognosis is cases in which on account of softness and vascularity a suspi-

FIG. 160.—Osteoma. (*Mears.*)

cion of sarcoma is aroused. In the case of the osteoma spongiosum the differential diagnosis may be difficult or easy according to the case. Only an overwhelming disproportion of cells not seemingly engaged in bone formation will suggest sarcoma. To test the excessive vegetative activity of the presumably superfluous cells, mitotic figures, deformed and gigantic nuclei, upon which the French school lay stress, may be sought for.

LIPOMA

A lipoma is a tumor composed of adipose tissue. In some cases predisposition to it seems to be hereditary and in rare cases the tumor is congenital. The tumor is usually single, but may be multiple, and when so, symmetrical. Homologous lipomas arise from adipose tissue, and occur where it is normally present; heterologous lipomas may be looked upon as embryonal displacements. The lipoma forms a more or less rounded, usually more or less lobulated, soft mass, surrounded by a distinct capsule, and composed of fairly uniformly yellow fatty tissue.

Care should be taken to differentiate between lipoma and lipomatoid formations, as shown in the following tabulation:

I. Lipomatoids.
  Adipose replacement hyperplasia.
    Pseudohypertrophia lipomatosa.
    Lipoma capsulare renis.
  Lipoma annulare colli.
  Steatopygea.
  Adiposus dolorosa.
  Polysarcia.
II. *Lipoma.* A definitely circumscribed new growth of adipose tissue.
  A. Clinical Varieties.
      1. Subcutaneous.
      2. Submucous.
      3. Subserous.
      4. Subsynovial.
      5. Intermuscular.
      6. Intramuscular.
      7. Meningeal.
      8. Parosteal.
      9. Renal.
      10. Uterine.
      11. Cardiac.
      12. Mediastinal.
      13. Myelogenous.
  B. Pathological Varieties.
      1. Lipoma.
      2. Lipoma fibrosum.
      3. Lipoma durum.   (Steatoma.)
      4. Lipoma myxomatodes.   (Collonema.)
      5. Lipoma telangiectaticum sue cavernosum.
      6. Lipoma petrificium ossificans.
      7. Lipoma cysticum.

In mammalian embryos the fat cells early differentiate themselves from the other mesenchymal cells and become distributed over the surface of the body to accumulate in certain of its recesses in the form of gland-like structures sometimes spoken of as the organs of Toldt.   In certain of the lower vertebrates the cells thus remain, but in man they gradually extend from these original foci until they generally pervade the subcutaneous fascia.   In the embryo these cells are more or less cuobidal in shape, have considerable cytoplasm, and present a distinctly epithelial appearance.   Soon after birth they begin to accumulate fat which first appears in the form of small scattered droplets, which grow larger and coalesce until a single large drop is formed, which then keeps on enlarging until the distended cytoplasm forms only a delicate envelope about it.

Adipose tissue is composed of great quantities of such cells closely packed together, the surfaces of contact being flattened by the mutual pressure, and the nuclei, compressed and inconspicuous, lying for the most part in the angles of the contacting surfaces.   Through such cellular fatty tissue—adipose tissue— bundles of fibrillar connective tissue pass accompanying the blood-vessels and lymphatics.   If the fat becomes absorbed the vacuoles become smaller, and the cells gradually return to the embryonal form and appearance.

A rather prevalent error seems to ascribe fat storage to any of the cells of the fibrillar tissue.   Mallory expresses himself very clearly upon this point when he

says: "The fat cell is not a fibroblast, is not derived from one, and in emaciation does not return into one."

If the fat storing cells of the entire body load themselves with fat, an enormous increase in size and weight results, the condition being described as *obesity* or *polysarcia*. If the distribution of the fat is less regular, excesses sometimes appear about the shoulders, hips, thighs, mammae, or the omental and mesenteric tissues with destruction of body symmetry, which, when it becomes extreme is called *steatopygea*.

Fig. 161.—Irregularly generalized adipose deposits in a case of lipo-dystrophy in the Philadelphia General Hospital. The deformity produced is known as steatopygea. (*Dr. F. G. Weisenburg*.)

In some cases the adipose deposits are nodular, and clinical experience shows that a few such cases are attended by sensitivity and pain, as though there was some relation between the nodules of adipose tissue and the nerves.

Dercum has called this condition *adiposis dolorosa*.

In some cases, without any general obesity, local collections of adipose tissue occur in restricted areas, but without circumscription or encapsulation. One of the most peculiar of these occupies the back of the neck, where it forms a roll of fat that hangs down over the collar. It is called *lipoma annulare colli*. Not infrequently the skin is covered with fine hair, which gives the appearance of a fur boa worn about the neck.

Other localized fatty deposits are symmetrical. Jonon, in the Revue d' anthropologia, 1908, xix, 459, gives a photograph of a man upon whose abdomen a cylindrical roll of adipose tissue crosses the mid-line above the umbilicus, a second twice as large below the umbilicus, while a third of quadrilateral form arising near the pubes, hung down so as to cover the external genitalia.

FIG. 162.—Lipoma a n n u l a r e colli.
(*Brophy*.)

Sailer at the Philadelphia General Hospital, had among his patients, a man appearing to be about 40 years of age, of feminine habitus, in each of whose large pendulous mammae was a mass of adipose, externally and symmetrically situated and extending toward the axillae. He also had a roll of adipose tissue encircling the anterior aspect of the neck below the chin, and a rounded mass as large as a man's fist on each side above the pubes.

Internal deposits occur in much the same way, sometimes confined to the omentum, sometimes to the peri-renal region, especially in cases of arteriosclerotic atrophy. Not infrequently large masses occur in the region of the pancreas, invading its substance and widely separating its lobules, some of which undergo atrophy. Retro-peritoneal fatty masses occasionally occur in the anterior abdominal wall near the inguinal canals, into which they sometimes penetrate for some distance, so as to become confused with hernias. Or they may occur posteriorly, high up, forcing their way between the crura of the diaphragm into the posterior mediastinum. Considerable and disproportionate accumulations of fat in the mesentery and omentum are too frequent to merit particular attention. These are all localized, uncircumscribed, and unincapsulated, and therefore not tumors, though sometimes spoken of as *diffuse lipomas*.

More definitely circumscribed fatty formations result from excessive deposits of fatty tissue in the epiploic appendages, and are sometimes regarded as lipomas, but their origin shows them not to differ from the other local deposits.

In marked contrast with all these is the true lipoma. Wherever it occur it always forms a distinct and independent entity, shut in by its capsule. It usually has a rounded and lobulated form, soft and almost fluctuating consistence, and a yellow color on sections.

The yellowness of the lipoma varies, probably according to the different proportions of olein, stearin and palmatin it contains. In a few cases different lobules of the same tumor, or adjacent tumors, differ in color, some being bright yellow, some almost white.

In almost all cases an incision over a lipoma enables it to be "shelled out" without difficulty. When this is done, the tumor is rarely heard from again, but in rare cases it recurs although nothing about it suggested such a probability. One such tumor recently under observation recurred seven times in fifteen years. It grew, deeply situated among the muscles of the thigh, of a middle aged woman. As the surgeon believed that he removed all of the capsule with the tumor, the

FIG. 163.—Man with symmetrical lipomas in both gynecomastic breasts and in both suprapubic regions. (*From a patient in the Philadelphia General Hospital.*) (*Sailer.*)

question from what the recurrence took place became an interesting one. It is possible that it was not from any residual part of the original tumor, but from other tumor primordia located near by.

Lipomas may occur at any age. They are not infrequently congenital. Except for a few curious fatty formations such as the "sucking cushion" described by Sutton as occurring between the masseter and buccinator muscles of emaciated children, the congenital lipomas in no manner differ from those that are acquired.

The tumors grow with varying rapidity.   In some cases so slowly that the patient notices no change in many years, and becoming accustomed to its presence, forgets all about it.   In other cases, growth is rapid and an enormous size may be attained.   The largest reported tumor, that published by Buckner in the Ohio State Medical Society's Transactions for 1851, and later by Delamater in the Medical Gazette Aug. 1st, 1859, and frequently referred to as "Delamater's tumor," occurred in the abdomen of a white woman aged 36 years, was known to have existed for 16 years, and at the time of her death from infection through a superficial ulceration, was estimated to weigh 275 pounds.   The patient herself weighed only about 90 or 100 pounds. Wells in his Chemical Pathology speaks of another fatty tumor that weighed 69 pounds.

Fig. 164.—Lipoma of shoulder.

But the greater number are much smaller, and as they are easily removed are rarely permitted to grow larger than an apple or a cocoanut.

The subcutaneous lipomas are most frequent. When situated upon the scalp, they are soft, hemispherical, or flattened; when in regions where the skin is looser, they are rounded, and sometimes pedunculated and pendulous.   The congenital lipoma of the mid-spinal region is always suggestive of spina bifida occulta.

Sub-mucous lipomas are more rare.   An interesting one, always of small size occurs upon the conjunctiva, at the external corneo-scleral junction and is known to ophthalmologists as *pinguecula*. Small pedunculated lipomas also occasionally occur in the larynx. A frequent situation is the small intestine where they grow beneath the mucosa, and sometimes assume a polypoid form. They have been known to excite peristalsis and result in intussusception.

Upon careful scrutiny most sub-serous lipomas appear to belong to the class of lipomatoids; only occasionally do true lipomas occur.

Intermuscular lipomas are not common, but have a wide distribution.

Intramuscular lipomas occur most frequently in the deltoids, the biceps, and the recti abdominales.

Small heterotopic lipomas occasionally occur in the pia-arachnoid of the brain and spinal cord.

Lipomas occurring in the uterus, kidney, and beneath the periosteum of bones, are probably, more complex tumors in which adipose tissue is the most conspicuous element.

Sub-synovial lipomas are rare, and are usually peculiarly arborescent. They are supposed to result from enlargement of the synovial fringes, with penetration of fat from the subsynovial adipose tissue.   They ought, therefore, be grouped with the sub-serous lipomatoids rather than with the true tumors.

Small pedunculated subcutaneous lipomas, unchanged for many years, occasionally suffer unexpected interruption of the vascular supply and undergo retrogressive change by which the fat is liberated from its protoplasmic envelopes
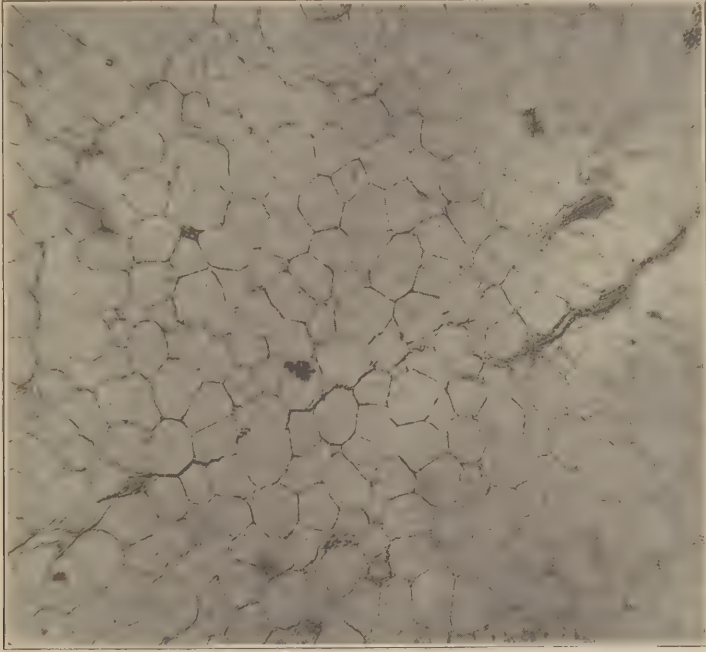
FIG. 165.—Microscopic section of a lipoma. (*Photomicrograph by Prof. Allen J. Smith.*)

and collects to form a kind of cyst, the *dermatocele*. Later precipitation of crystals of the fatty acids and cholesterin in such cysts may explain some of the "cholesteatomas" of the skin.

In occasional cases calcification of the fibrous trabeculae of the tumor is followed by ossification—*lipoma petrificium ossificans*. However, in such cases, it is not always possible to determine that the primordium from which the tumor grew was simple.

Uncomplicated lipoma is a perfectly benign tumor. Ordinarily it does not recur, and except it be in some manner mixed with sarcoma, does not cause metastasis. A few rare cases are recorded in which it is stated that uncomplicated lipoma has recurred, but there is always the suspicion that the tumor was lipo-sarcoma, and really malignant from the beginning. The

FIG. 166.—Large, pendulous subcutaneous lipoma of the neck.

same suspicion applies to cases in which the tumor is said to have "changed its disposition," and to have "acquired malignancy."

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The not infrequent occurrence of ulceration upon the surface of large lipomas has sometimes led to mistakes in diagnosis, malignant tumor being suspected, and unnecessary operations performed.

ANGIOMA

An angioma is a tumor whose essential component is newly formed blood or lymph vessels.

Adami is undoubtedly correct in insisting that a sharp line of separation ought to be made between vascular enlargements resulting from mere dilatation, and those resulting from new formation. The former are telangiectasias, not tumors, and should be called angiomatoids; the latter are true tumors arising from unipotent cells, angioblasts. But there is difficulty in the practical application of this principle because of the impossibility of determining through which process any given vascular tumor originated.

Ewing points out "that vessels occupy an altruistic position in the physiology of organs, subordinating themselves to more specialized structures." In beginning the study of tumors attention was called to the peculiar manner in which, regardless, of the independence arising from encapsulation, every one was obliged to provide for its nutrition by calling into its own substance, from the surrounding tissues, enough vessels to maintain it, and to determine, in some peculiar manner, that these vessels enlarged and proliferated as its growth made necessary. This is in obedience to a general physiological law. If a tissue becomes active, its blood supply must at once be increased; if it grows, new vessels must be formed. In the growing granulation tissue of healing wounds, new capillaries are formed to supply the temporary need, and some granulation tissues are much more vascular than others. Some form of stimulation seems to determine how many new vessels shall form, but whether it be through direct or indirect stimulation of the preexisting vessels is not known. New growth of blood-vessels leading to angioma, must be the result of some similar stimulus, in which respect angioma is like other tumors; but a difference between angioma and other tumors is the lack of a definite primordium from which the tumor should grow. The tissues of other tumors are independent of the normal tissues. the vessels of angioma communicate with the pre-existing vessels, and, indeed seem to be extensions from them. But almost every angioma consists of something more than vessels; between them is intervascular substance in varying quantity. In some cases it is the remains of the tissue in which the tumor grows, in others it is a new fibro-cellular tissue. In many cases it is so insignificant as to be negligible but in others it becomes conspicuous, and may assume great importance, connecting the vascular tumors with the cellular tumors—sarcomas. In the former case it seems improbable that the increase in vascular structure can depend upon the stimulation of this intervascular stroma, but in the latter, it is highly probable. Especially is this true of those vascular and cellular tumors that are malignant, and in whose metastatic secondaries the same proportion between vessels and stroma is maintained.

In granulation tissue, to which reference has already been made, the formation of the new vessels seems to take place through the activity of the capillary

endothelium, the cells of which, now commonly spoken of as angioblasts, penetrate into the delicate reticulated and usually fibrinous exudate as a succession of elongated cells that subsequently become canallated and so transformed into a capillary. If this is destined to be the parent of numerous additional vessels, muscle cells and fibroblasts follow the endothelium from the larger vessel with which it connects, and it becomes a complete vessel.

FIG. 167.—Microscopic section through a hemorrhoid showing the dilated veins, filled with blood, of which it is composed. It is a telangiectasia, not an angioma. (*Photomicrograph by Dr. F. D. Weidman.*)

Mallory looks upon angioma as a product of endothelioblasts, and regards all angiomas as endotheliomas, calling them angio-endothelioblastomas.

Many other writers share this opinion, which perhaps affords the best explanation of many of the peculiar histological appearances observed in different tumors, as well as accounting for the peculiar manner in which multiple forms occur.

It seems quite clear that angioblasts are either endothelial cells or derivatives from them, and that the new vessels arise through their multiplication. Should they develop activities corresponding with those of other cells engaging in tumor growth, angioma would be the result, and its variations no more than tumor variation in other tissues.

If a series of angiomas be histologically examined, some of the vessels will be found to have quite perfect walls, representing typical vascular formation, while others will show a variety of appearances indicative of imperfect formation, the most striking being endothelium in several layers, tending to accumulate in masses at intervals.

Ribbert's researches upon the blood-vessel tumors indicate that all of the overgrowth takes place in the distribution of a single vessel. Into the mass a single artery enters, and from it a single vein passes. No matter how large the tumor mass, it seems to have no communications with neighboring vessels. New branchings, lengthening, dilatation and tortuosity of the vessels lie at the foundation of all vascular tumors. Sometimes these take place in so well localized an area as to constitute a mass by which the pre-existing structures are extinguished by pressure atrophy, or pushed aside as in benign tumor growth, so that a capsule may be formed. At other times the growth ramifies for considerable distances in various directions. In the first case it is easy to recognize a tumor; in the second impossible. Thus the vascular tumors blend into telangiectases.

As there are two systems of vessels, it is customary to make two divisions of vascular tumors, *hemangiomas*, which develop from the blood-vessels, and *lymphangiomas*, that arise from the lymph vessels. The content and clinical manifestations are the chief differences between the two. They probably originate and grow in much the same manner.

The relations, varieties and clinical forms of these tumors are suggested by the following tabulation:

A. Angiomatoids.
    Lymphangiectasis in elephantiasis.
    Varicose aneurysm.
    Cirsoid aneurysm.
   Vascular hypertrophies.
    Naevus vasculosis.
   Telangiectasias.
    Senile angiomas of the skin.
    Hemorrhoids.
    Racemose angioma.
    Plexiform angioma.
B. Angioma.—A vascular tumor.
   I. Hemangioma—blood-vessel tumor.
      Angioma simplex.
      Naevus vasculosis.
      Naevus flammeus.
      Angioma cavernosum.
      Hemangio-endothelioma.
   II. Lymphangioma—lymph-vessel tumor.
     Pathological varieties.
       Lymphangioma simplex.
       Lymphangioma cavernosum.
       Lymphangioma cystoides.
       Lymphangioma hypertrophicum.
       Lymphangio-endothelioma.

Clinical varieties.
    Cystic hygroma.
    Makroglossia.
    Makrocheilia.
    Lymphangioma tuberosum multiplex.

It will be noted that Naevus vasculosis appears both as a tumor and as a telangiectasia. It is thus introduced to emphasize the difficulty of classification, and the differences of opinion in regard to its nature.

The great majority of vascular tumors are congenital. Indeed, in the minds of many, it is a question whether any are really acquired, or whether all do not grow from inconspicuous beginnings that were present at birth, but overlooked.

It now becomes necessary to separate the blood-vessel and lymph-vessel tumors, in order that the peculiarities of each may be considered.

<div align="center">HEMANGIOMA</div>

I. *Angioma Simplex*, also called *Naevus Vasculosis*.—This is a congenital tumor or telangiectasia, according to the authority accepted, well known as the "birth-mark" or "mother's mark."

FIG. 168.—Angioma of lower lip.

FIG. 169.—Angioma of upper lip. (*Dandridge.*)

It appears in the form of an elevated reddish or purplish discoloration associated with more or less hypertrophy of the skin. In most cases the lesions are small, but they may cover a square foot or more of the skin surface. When the color is bright red, they are frequently spoken of as *naevus flammeus;* when dark purple, as "port wine stains." There is no essential difference between the two, each consisting of more or less dilated capillaries in the cutis. The skin covering the discoloration may be normal, or thick, rough, and covered

with nodular and warty formations, some of which may be as large as a pea. Not infrequently the surface is covered with lanugo hairs, or scattered coarse and long hairs.

Whether occurring before, or shortly after birth, these discolorations are likely to remain throughout the whole life of the individual. In rare cases they disappear; in more frequent cases they enlarge. According to Stephen Paget the pale and slightly raised naevi are most likely to disappear, but Crocker has seen a port wine stain do the same. The disappearance is the result of a slow form of ulceration beginning at the periphery and gradually extending toward the center. Over the ulcerated surface crusts form, from time to time separating, each time leaving the lesion smaller, until only a pale scar remains.

FIG. 170. Photograph of hemangioma of the stomach as it presented on the mucous surface. (*Lemon.*)

When sections of the skin affected are studied histologically, the capillaries about the hair follicles, sweat glands, sebaceous glands and of the papillae, as well as many of those of the surrounding adipose tissue are found to be dilated, elongated and tortuous so as to form closely compacted vascular plexuses with more or less dilated spaces.

II. *Cavernous Angioma.*—This is generally conceded to be a true tumor with actual new formation of blood vessels. Mallory thinks that its growth begins in the veins rather than in the capillaries, at first taking the form of endothelial folds supported by a small amount of connective tissue, and resembling the valves of the normal veins. Continuing to grow, these become thrown into numerous folds which obstruct and dilate the vessels until their walls give way to the pressure, and permit the angioblastic mass to escape and invade the adjacent tissues. Such growths are frequently multiple, and appear simultaneously or successively in parts of the body in such relation to one another

Fig. 171.—Cavernous hemangioma in a girl fourteen years old. (*Mallory* "*Principles of Pathologic Histology.*")

Fig. 172.—Cavernous hemangioma extending within a vein. (*Mallory,* "*Principles of Pathologic Histology.*")

as to make metastasis out of the question.   Mallory has published a photograph
of a 14-year old girl with an angioma that first appeared in the axilla, but later
continued to grow down the arm to the fingers which became transformed
into almost shapeless masses of closely approximated angiomatous nodules
at the same time similar tumors appeared on the thoracic wall.   Ewing figures
a woman with an angioma of the left mamma, and later appearing nodules at
the jaw, neck and right axilla.   The distribution in these cases certainly did
not take place either through the lymphatics or the veins, as in tumor metastasis

Fig. 173.—Metastasizing angioma of left breast.   Note tumors of jaw, neck, under ear,
and at right axilla.   There were tumors also in the pharynx and in the lungs.   (*Ewing,*
"*Neoplastic Diseases.*")

generally, and it is difficult to imagine it to have occurred by way of the arteries.
Such cases are different from the occasional truly metastatic angiomas.   Thus
Borrmann has reported an angioma of the skin of the breast that repeatedly
recurred locally, then later become metastatic, and filled both lungs with
secondary tumors.

    Superficial cavernous angiomas occur in the skin and subcutaneous tissues,
especially of the lip, ear, external genitalia, folds of the axillae, knees, and
buttocks.   They also occur in the sub-mucous tissue, especially of the tongue.
They may resemble the angioma simplex, but are usually much more elevated,

and their surface more nodular. They tend to enlarge and are predisposed to hemorrhage from rupture of the distended superficial vessels if subjected to the slightest traumatic injury.

Deeper tumors of this kind occur in nearly all of the organs—liver, spleen, kidney, uterus, brain and spinal cord, mamma, bladder wall, intestinal wall, muscle, cardiac wall, ovary, and bones. They also occur in the fascias, and

FIG. 174.—Metastasizing angioma, secondary nodules in the lung. (*Borrmann*.)

along the course of nerves—as in the cavernous angiomas of the orbit that follow the optic nerve from the retro-orbital adipose tissue into the globe of the eye.

To the naked eye these tumors present a great variety of appearances according to the size and dilatation of the vessels of which they are composed. Thus, in the lips, they form swellings of a deep purple color, usually covered with smooth skin and mucous membrane. Elsewhere they form considerable sized elevations over which the skin may be smooth, but is more apt to be thickened and nodular. The color varies. It may be bright red, or deep purple when most of the vessels are near the surface, and slightly red or purple when they are deep. The tumors are compressible, but the blood quickly returns when the pressure is relieved. Large tumors may pulsate.

The deep angiomas are characterized by spongy vascular structure and purple color. In rare instances angiomas are encapsulated; in a somewhat

larger number they are well circumscribed, but in most cases they have ramifications that extend widely into the neighboring tissues, so as to make their surgical removal by dissection difficult and frequently impossible.

The histological structure of this form of the tumor does not differ essentially from the other, but the vessels are larger, more widely dilated, and frequently show alteration of the endothelium which may assume a cuboidal shape, or occur in several layers—*hemangioma hypertrophicum.*

In general, angioma is a benign tumor. It is, however, destructive in tendency because of the crowding out of the normal tissues by the ever enlarging and increasing blood-vessels. In a few cases recovery occurs as the result of thrombosis following injury and most of the measures by which the tumor is at present treated, are directed toward the production of thrombosis in the hope of effecting subsequent organization.

LYMPHANGIOMA

This tumor is derived from the lymph vessels, and is usually congenital. Clear separation of the tumor from the lymphangiectases is not always possible.

FIG. 175.—Cavernous lymphangioma of the axilla, of congenital origin. (*Warren.*)

The tumors present at birth are sometimes small, sometimes very large. If small, they may remain so, but usually they increase in size.

They are most frequent about the face and neck. In the former they cause enormous swelling of the eye-lids, lips, cheeks, or tongue.

The eye-lids become enormously thickened, and so heavy and pendulous that they cannot be raised; the cheeks hang loosely as jowls; the lips so thickened and deformed that the upper resembles a snout, and the lower hangs like the lip of a pitcher. This condition is known as *makrocheilia.*

When the tongue is affected, it either depresses the floor of the mouth making it appear as though the tumor was in the neck, or it protrudes from the mouth, everting the teeth, and deforming the alveolar processes, sometimes attaining to such an enormous size as to hang to the breast, an utterly useless organ with a dry fissured surface, inclined to bleed upon the slightest injury, and partly covered with crusts. This condition is called *makroglossia*.

In the neck, when they attain their largest size, they usually occur in the antero-lateral region, rarely ascending above a line drawn from the corner of

FIG. 176.—Congenital lymphangioma of the neck. (*Redrawn from Le Dentu and Delbet.*)

FIG. 177.—Congenital lymphangioma of the neck, deeply seated and divided by o v e r l y i n g muscles. Also called cystic hygroma. (*Redrawn from Le Dentu and Delbet.*)

the mouth to the angle of the jaw, but reaching to the external ear behind, to the sternum below, and passing beyond the middle line in front. In rare instances only do they occur posteriorly. They form soft compressible swellings, covered with smooth pale skin. When cystic they may fluctuate and are translucent by transmitted light. They do not swell when the child cries, nor can they be reduced.

Lymphangiomas also sometimes occur in the orbits, the mediastinal and retro-peritoneal tissues, and occasionally in the intermuscular fascia.

Although the tumor is frequently divided by bands of fibrillar tissue it is rarely sharply circumscribed, and probably never encapsulated. It commonly has lengthy extensions that fill the intermuscular spaces, and follow the lines of the vessels with which it is frequently in intimate relation.

When such a tumor is cut, it appears, to the naked eye, to have a peculiar spongy or frothy appearance, because of the innumerable spaces, large and small that it contains, and from which the lymph escapes leaving only the delicate framework between the dilated vessels.

Several incisions into such a tumor sometimes result in its almost complete disappearance through collapse. When the lymph spaces are large they may

close and form real cysts, some of which are as large as a walnut.   Tumors
with distinct cystic structure are sometimes called *cystic hygroma*.

Some of the cysts intercommunicate, others do not.   Langhans was able
to trace colored fluids injected into the efferent lymph vessel, into some of
the cysts.   But they do not all communicate as can easily be determined in
cases in which the tumor has sustained traumatic injury, or become infected,

FIG. 178.—Cavernous lymphangioma of neck and axilla in a young woman.   (*Homan.*)

for then some, but not all, of the cysts may contain bloody fluid or pus.   It is
not unusual to observe tumors in which some of the cysts are filled with clear
lymph, others with bloody fluid, and others with milky or purulent fluid.

According to the histological structure Wegner has divided the tumors into
three groups; *lymphangioma simplex*, in which there are anastomosing vessels
and spaces of small size; *lymphagioma cavernosum*, in which the vessels are of
large size and form a closed system, and *lymphangioma cystoides*, in which there
is a congeries of large and small cysts filled for the most part with clear lymph,
and not communicating.

In all cases the spaces are divided by septa of varying thickness.   There
being no definite walls to the lymph spaces, the thickness of the septa bears no

relation to the size of the spaces. In lymphangioma simplex the endothelial cells lining the relatively small vessels and spaces are frequently cuboidal; in the other varieties, with the relatively larger spaces and cysts, the cells are flattened. The presence of several layers of cells, marks the beginning of the condition described as *lymphangioma hypertrophicum*. With increase in the number of these cells the tumor connects with the angio-sarcomas, and leads into the malignant tumors.

Between the vessels and cysts of lymphangioma there are sometimes islets of adipose tissue, strands of striated muscle and occasional bits of cartilage.

FIG. 179.—Lymphangioma of the thigh and adjacent parts. (*Dr. F. D. Weidman.*)

Their presence is suggestive of mixed tumor, but is generally interpreted to indicate that the formation of the tumor began at a time prior to that at which the differentiation of the tissues became clear, so that individual components became separated and some of them included in the substance of the tumor.

Of 126 cases of lymphangioma collected by Dowd, 91 were situated in the neck, mostly in its anterior region.

It is said that when small they were sometimes mistaken for branchiomas (branchial cysts) or for enlarged lymph nodes. It is difficult to see how that could happen as the former do not appear for some time after birth, and the latter should be hard.

Lymphangiomas are benign tumors, usually occurring singly, but occasionally multiply, as in the case of hemangioma. Their growth and consequent disfigurement makes removal desirable, and as the operation is free from the risk of hemorrhage it is frequently undertaken with success.
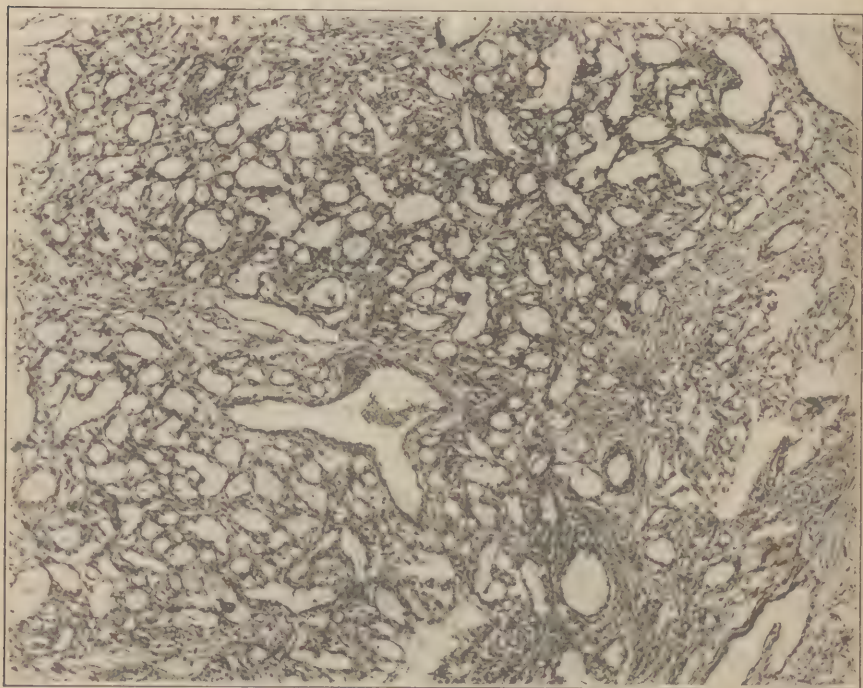
FIG. 180.—Microscope section of a lymphangioma of the nose.

ENDOTHELIOMA

An endothelioma is a tumor that arises from endothelium. Presumably, therefore, it may originate from the blood or lymph vessels or from the serous membranes.

Endothelium, under normal conditions, is nearly always composed of large flattened cells, characterized by transparent cytoplasm almost free of granules and containing relatively small vesicular nuclei with little chromatin so disposed as to resemble dot-like nucleoli. In this form, and in a single layer, it forms the lining of the larger blood-vessels, forms the smaller blood and lymph vessels and covers the surfaces of the serous membranes. The only activities manifested under conditions that may be regarded as physiological, are vascular new formation on the part of the vascular endothelium, and limited regenerative vegetation on the part of the mesothelial endothelium. Its reactions are, therefore few and distinctly limited.

As the tumors resulting from the angioblastic activity of the endothelium are chiefly characterized by newly formed vessels, it has been thought wise to class them as vascular tumors, even though upon occasion some excess of endothelium

may be present in the walls of those vessels. On that account angioma, lymph-angioma, hemangio-endothelioma and lymphangioendothelioma have been considered in the preceding sections. But many authorities prefer to class them among the endotheliomas, and Mallory regards all vascular tumors as endotheliomas.

At the present time there seems to have crept into the literature of pathology the wide-spread opinion that endothelium is a versatile and modifiable tissue,

FIG. 181.—Lymphangioma of the tongue. (*New.*)

capable, through anaplasia and metaplasia, of transmutation into many other types of tissue, and so giving rise to tumors of varied histological appearance.

For this opinion there seems to be little justification, and with it we are entirely out of sympathy. It has led to the assignment of a large number of non-de-script tumors to the class of endotheliomas for no other reason than that they were of unknown origin, peculiar structure, and difficult classification

So long as one is of the opinion that endothelium may be fibroblastic, or assume the appearance of epithelium—columnar, cuboidal or glandular—this is not inconsistent, but it does not seem scientific unless there is real evidence in support of it.

The following tabulation shows the tumors most regularly assigned to the class of endotheliomas:

Endothelioma.
    I. Angioblastic.
        Hemangioma.
        Hemangio-endothelioma.
        Lymphangioma.

       Lymphangio-endothelioma.
       Angio-sarcoma.
          Perithelioma.
          Cylindroma.
          Psammoma.
          Cholesteatoma.
   II. Mesothelial.
          Endothelioma.
             (Endothelial cancer).
   III. Meningeal.
          Dural endothelioma.
   IV. Mixed tumors.

Of the angioblastic group, the vascular tumors have already been considered, and the sarcomas will be taken up later. The mixed tumors have been dwelt upon in the section upon Congenital Diseases of Surgical Importance, and need no further discussion here. There, therefore remain for consideration two tumors, the dural and the mesothelial endotheliomas.

Ewing, who follows Borst in believing that the scope of endothelioma is probably very wide, gives the following:

HISTOLOGICAL TYPES OF ENDOTHELIOMA

1. *Interfascicular Endotheliomas.*—The cells grow in thin layers between strands of connective tissue. When these strands are swollen and hyaline the tumor may be designated as cylindroma.

2. *Alveolar Endothelioma.*—The cells grow in small or large groups, as in adenoma. When appearing in long sections the groups may be tubular. When mucinous degeneration occurs in these cell groups a variety of cylindroma is produced, but the use of this term for such structures, leads to confusion and is inadvisable.

3. *Plexiform Endothelioma.*—The cells grow in convoluted columns often surrounding vascular paths. Papillary projections may arise from these columns suggesting the term papillary endothelioma. This structure is represented by several tumors of doubtful origin.

4. *Perivascular Endothelioma.*—The cells surround definite vascular paths usually in concentric fashion, as in the dura mater. *Psammoma* or sand tumor, applies to this growth when the units are calcified. Osteo-endothelioma forms rarely in the same manner (Parthes).

5. *Diffuse Endothelioma.*—The cells grow diffusely without any definite arrangement in uniform relations.

6. Miscellaneous changes in the stroma, progressive and regressive, are readily indicated by appropriate terms as osteo, myxo, fibro, cysto, etc.

   Perithelioma, whatever its origin, is a highly characteristic structure which exhibits the qualities of sarcoma or carcinoma, with which groups it should be classed.

But with respect to these tumors one is far from being upon solid ground with reference to their derivation from endothelium.

The dural endothelioma occurs in the form of single or multiple, more or less regularly rounded, sometimes hemispherical masses, that arise by a broad base from the inner surface of the dura and its related pia-arachnoid. Each is sharply circumscribed, though not encapsulated, is usually loosely attached to the dura, and scarcely attached to the pia-arachnoid. The size varies from a pea to an egg, and space is obtained at the expense of the brain substance which is

FIG. 182.—Endothelioma of the meninges lying in a deep depression in the surface of the cerebral hemisphere. (*MacCallum, "Text-book of Pathology."*)
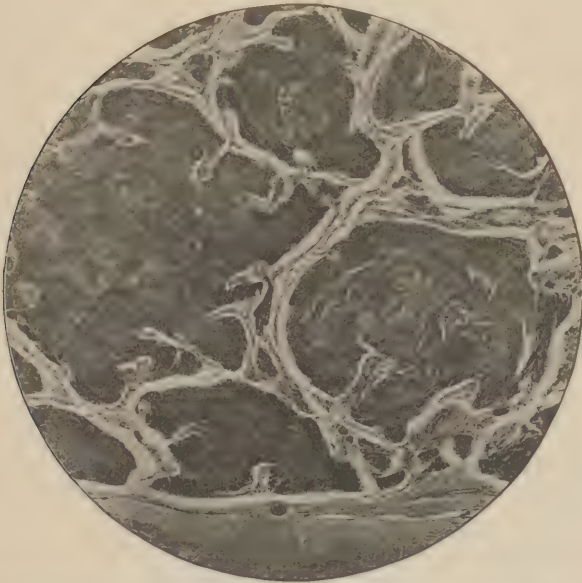
FIG. 183.—Dural endothelioma. Cells form large whorls. Dura at base of picture. (*Mallory.*)

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compressed, and occasionally through added atrophy of the supra-jacent bones of the cranium. The tumor may be smooth or lobulated, and soft or firm according to its nutritive condition. It is nourished by vessels derived from the dura, and the degree of lobulation depends largely upon their distribution. The color is grayish or pinkish gray.

The tumor is most common upon the convex surface of the cerebrum, but may arise from the falx, the tentorium, more rarely about the vessels at the base of the brain, and still more rarely about the medulla. It also sometimes
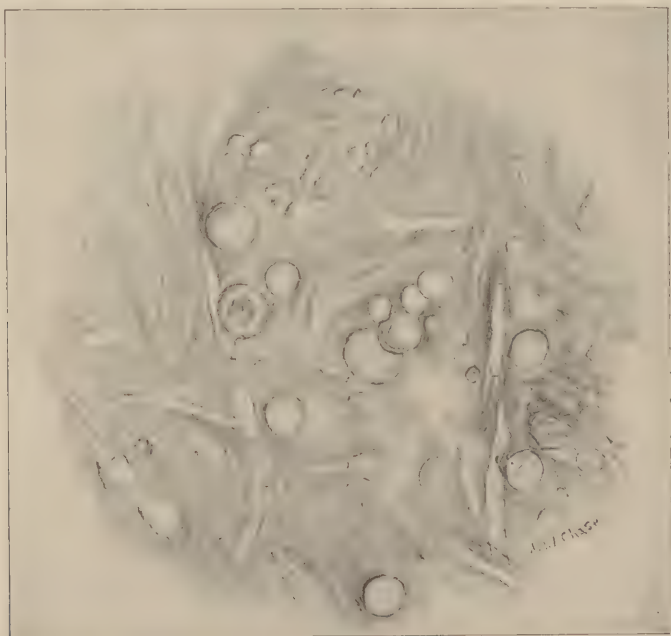
FIG. 184.—Psammoma. The matrix of the tumor consists of a degenerated fibrous tissue in which are numerous spheric and cylindric mineral masses.

occurs upon the membranes of the spinal cord, especially in the middle and lower thirds. Supposedly similar tumors have occasionally been encountered in the ventricular cavities, where they are supposed to take origin from the pia.

When examined histologically, the tumor is found to be composed of cells of distinctly spindle shape, arranged with long diameters parallel, and showing a distinct disposition to form whorls about the blood-vessels, so that the section shows many little knots, some of which undergo hyaline change, and some of which calcify with the formation of chalcospherites. Tumors containing many of these are frequently designated *psammomas*.

The tumors grow very slowly, remain local, and do no harm other than that which results from pressure upon the brain and bones. In rare cases the dura becomes invaded, the spindle cells separating its fibres. If operatively removed, this tumor rarely recurs, and metastasis is almost unknown. Klebs saw a case in which there were nodules in the lung, and Lindner one with metastasis to the bladder. But in these cases, there may have been a mistake in diagnosis.
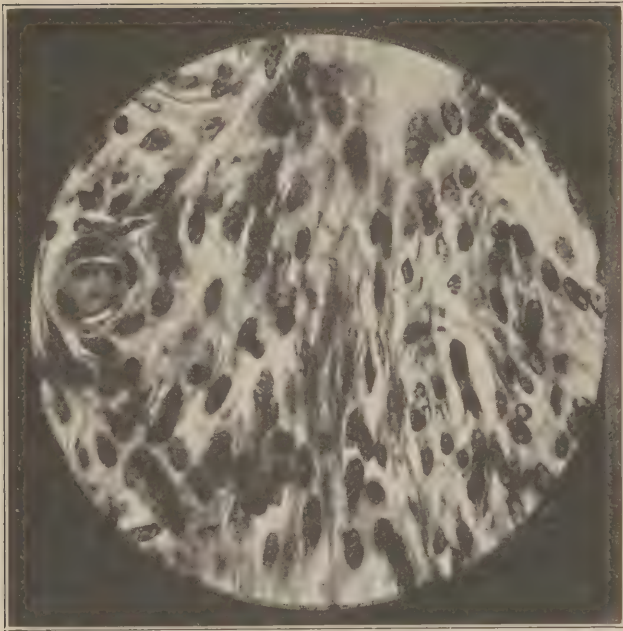
Fig. 185.—Microscopic section of a dural endothelioma showing the fibroblastic structure, and numerous fibroglia fibrils. × about 600 diameters. (*Mallory.*)
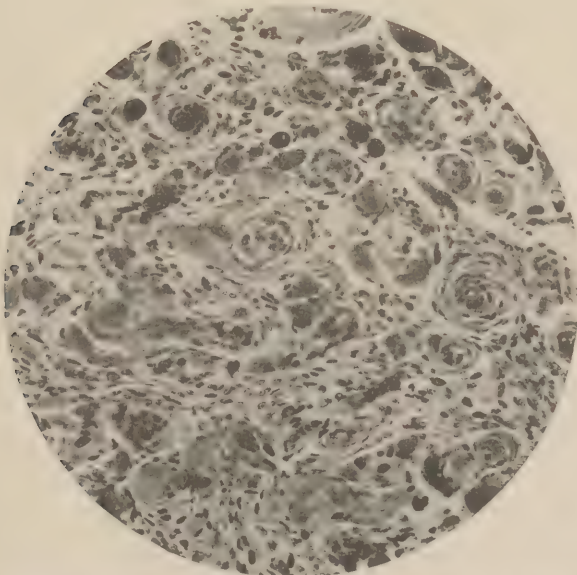
Fig. 186.—Dural endothelioma containing numerous whorls formed around hyaline masses of collagen fibrils. (*Mallory.*)

A careful study of these tumors was made, by Mallory, in 1920, and his conclusions are most important. In the first place he could not find that the dura had an endothelium lining as was previously supposed, so that it seems to be impossible for the tumor to have the origin formerly ascribed to it. In the second place, he showed that the tumor is not composed of endothelial cells, but of fibroblasts derived from the superficial cells of the pia-arachnoid. He says:
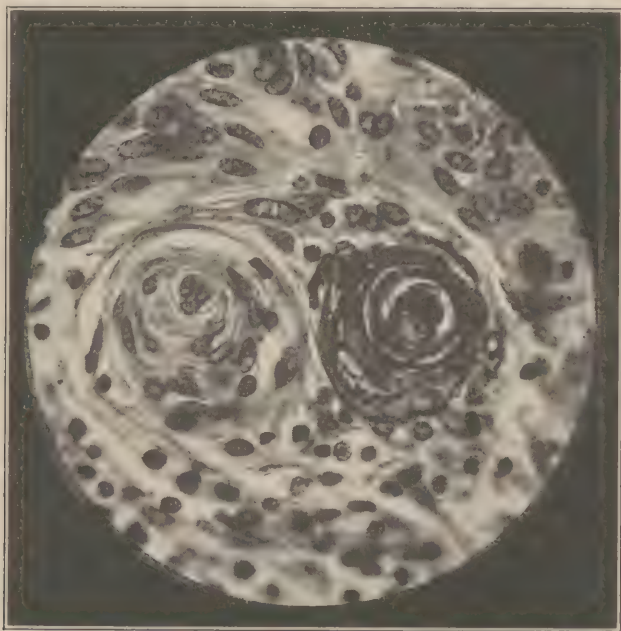
Fig. 187.—Microscopic section of a dural endothelioma, showing one whorl composed of cells, and another chiefly made up of fibers. × about 600 diameters. (*Mallory*.)

"The arachnoid early exhibits two characteristics which seem to be peculiar to it. Its free surface towards the dura develops a layer of cells resembling endothelium, the so-called dural endothelium. These cells instead of multiplying evenly all over the surface usually proliferate in foci, so that groups of dozens, or even hundreds of cells occur here and there.

They may form focal layers up to a dozen or more layers in thickness. As these cells get older they develop fibroglia, collagen and occasionally elastic fibrils. This method of growth of the arachnoid leads to irregular thickening of the membrane. The second peculiarity of the arachnoid is that the collagen fibrils are not very abundant in comparison with the number of cells, and that they do not form compact strands, but remain more or less separated from one another. In other words, the arachnoid cells are not so highly differentiated fibroblasts as those which form the dura.

In view of the foregoing statements of the nature and origin of the arachnoid membrane and of the peculiar character of the cells lining its outer surface, it seems fairly evident that the tumor known as dural endothelioma is incorrectly named. It should be recognized in the future as one type of fibroblastoma and named accordingly—*arachnoid fibroblastoma*."

Mallory also shows in the same paper that the Pacchionian granulation is not, as supposed by Ribbert and others, derived from the dural endothelium, but from these same cells of the arachnoid, and that they have the same essen-

tial structure. He also connects the so-called dural endothelioma with the perineural fibroblastoma, through the continuous or interrupted growth of the same fibroblastic tissue along the nerves, and speculates whether neuro-fibroma molluscum may not be related to both.

If Mallory be correct and there is no dural endothelioma, the only tumor left in the group is the mesothelial endothelioma (endothelial cancer) occurring upon the serous membranes of the pleura and peritoneum.

These tumors are rather rare, and occur as single or multiple, pale, flattened, discrete or partly confluent, well circumscribed, firm and frequently cicatricial formations scattered over more or less extensive surfaces of the pleura or peritoneum. In rarer cases the multiple growths are sensile or polypoid and rounded. The surface may be smooth, covered by a thickened membrane, or rough and sometimes adherent to the opposed surface. The tumor is of slow growth, and there is very rarely evidence of metastasis. The affected membrane is sometimes greatly thickened, dense and scirrhus, and when cut, shows a variegated appearance resembling cancer.
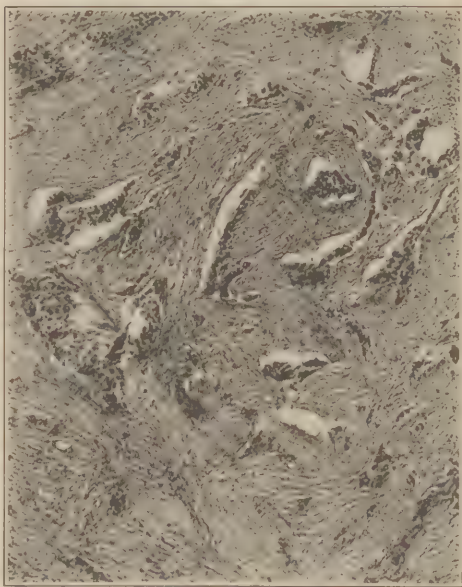
FIG. 188.—Endothelioma of the pleura. The resemblance to carcinoma cannot fail to strike the observer.

When this tumor is examined histologically, it is found to resemble carcinoma —so much so that it is not infrequently called *endothelial carcinoma*. The resemblance is not usually dwelt upon however. The reverse is probably true; the resemblance is neglected, or even denied on account of the preconceived theory which supposes it to be impossible for the tumor to be carcinoma, as it arises where no epithelium from which it could originate, should be present.

The histological resemblance to carcinoma is in many cases, striking and if the source of the material under examination were unknown, in most cases it would probably be called cancer. In Borst's case in which there were epithelial pearls, scarcely any other diagnosis would be possible.

But it is generally supposed that this tumor arises from the endothelial cells, of the surface of the membrane in which it grows, or from those of its lymph channels. Its true histogenesis is not known. The theory of tumor origin to which the student adheres, determines how he will regard it. If he believes that carcinoma always develops from a primordium consisting of glandular or surface epithelium, he will reason that it cannot be carcinoma because of the absence of such a primordium in the vicinity; if, on the other hand, he assumes that

carcinoma may arise from disseminated and sequestered germinal cells, as supposed by Rottner, he may see no objection to supposing that a tumor whose structure is so definitely that of carcinoma is what it seems to be.

A remaining group of tumors regarded as endotheliomas occurs in the bones, and has recently attracted attention on account of susceptibility to the destruc-

FIG. 189.—Angio-endothelioma of humerus.
(*Ewing.*)

tive action of radium and X-rays, which enables many of them to be successfully treated without amputation. They are histologically characterized by the presence of great numbers of large, clear, endothelial-like cells, or small polyhedral cells with clear cytoplasm, that distribute through the marrow, or other structure, in sheets, cords or columns, without intervening stroma, sometimes tending to form alveoli, and prone to mucinoid degeneration with the formation of cysts.

They are sometimes multiple, sometimes solitary, sometimes circumscribed, sometimes diffuse. They destroy the bone, replacing it by their own substance, without new bone formation. Allowed to go untreated they sometimes cause metastatic tumors.

The endothelial nature of the cells of these tumors, some of which were formerly described as alveolar sarcomas, and some of which are called myelomas at present, is a matter of inference rather than of demonstration.

Ewing divides the endotheliomas of bone into three groups: (1) *Multiple endothelioma* which may affect nearly every bone in the body, whether as independent primary tumors, or as secondary tumors from one primary focus is not known. They occur only in adults, and the patients nearly all die. The lesions bear a certain resemblance to multiple myeloma, but do not so sharply penetrate the bone. (2) *Solitary angio-endothelioma*. This occurs chiefly in adults, as a simple tumor whose chief seat of occurrence seems to be the lower end of the humerus. It grows rapidly, completely destroys the bone, attains to a large size, and is pulsatile. It begins as a central tumor that distends and causes complete disappearance of the bone, not even being surrounded by a bony capsule, lying free within the periosteum. It returns after amputation, and gives metastasis. (3)

Diffuse endothelioma (solitary). This nearly always occurs before the 21st year of age, the bones affected being the ulna, tibia, pubes, radius, femur, scapula and skull. It begins with pain and develops slowly. It may recur after amputation, and may give metastasis. It, however, readily retrogresses under X-ray or radium treatment. It is commonly diagnosed myeloma and round cell sarcoma if the tissues be poorly fixed for microscopic examination. Some of Ewing's cases were thought "by competent observers" to have been osteomyelitis.
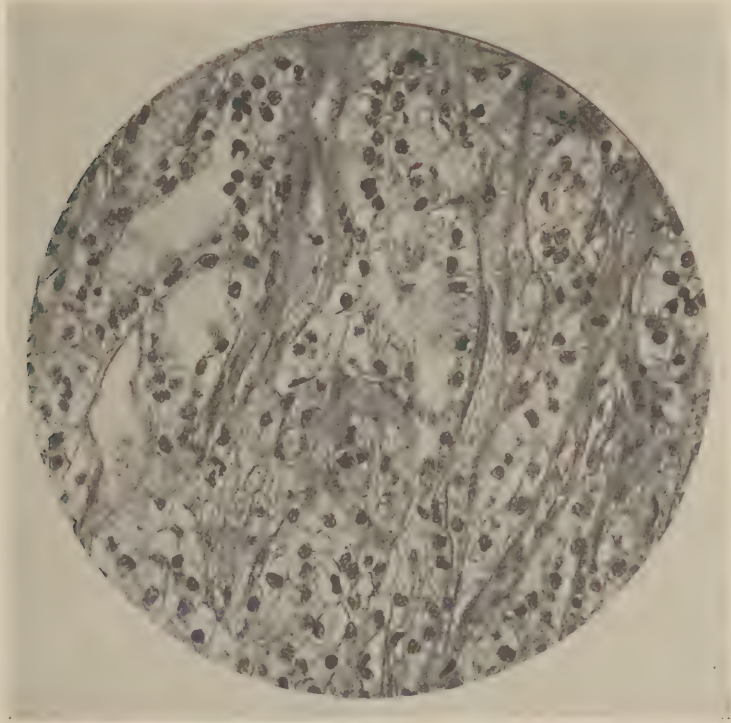
FIG. 190.—Structure of angio-endothelioma of bone. (*From Ewing, "Neoplastic Diseases."*)

The disease begins in the marrow or shaft or both, and the soft tissues are invaded after the bone is destroyed. X-ray examination shows the whole shaft of the bone or a long segment of the bone to be involved.

MYOMA

A myoma is a tumor composed essentially of muscular tissue. In nearly all cases it is composed of unstriated muscle; rarely of striated muscle. Its various forms are shown in the following tabulation:

Myomatoids.
Inflammatory hyperplasia of muscular tissue.
Hypertrophic elongation of the cervix uteri.
Adenomyometritis.

Adenomyosalpingitis.
   Salpingitis nodosa isthmica.
Certain enlargements of the prostate gland.
Congenital pyloric muscular hypertrophy.
II. *Myoma*.
   A. Myoma laevicellulare, or leiomyoma, the unstriated muscle tumor.
      Leiomyoma fibrosum.
      Leiomyoma durum.
      Leiomyoma cavernosum.
      Leiomyoma adenomatosum—Adenomyoma.
      Leiomyoma malignum.
   B. Myoma striocellulare, or rhabdomyoma, the striated muscle tumor.
      Congenital mixed tumor.

The myomatoid conditions are usually not difficult to differentiate from the true tumors, being characterized by the preceding clinical history of inflammation, the lack of circumscription, or both.

The leiomyoma is one of the most frequent and best known tumors, especially in its most common form, the uterine fibroid. This tumor appears in the form of rounded, more or less nodular, single or multiple, firm, embedded, sessile or pedunculated, well encapsulated growths, whose cut surfaces vary from reddish to pinkish gray in color, and are always distinctly fasciculated in texture. Ordinarily uniform, they may vary through the presence of areas of necrosis or degeneration, which for the most part appear as paler, and sometimes almost white areas, but which may form cysts filled with soft mucinoid contents, or may consist of calcareous deposits, and sometimes of bone.

Microscopic examination shows the tumors to be composed of parallel bundles of long spindle cells with rod-shaped nuclei, twisting and twining about the vascular axes, and separated by varying quantities of fibrillar connective tissue. Rapidly growing cells, have nuclei, which become more vesicular in appearance, and the cells themselves become broader, so that they may be confused with fibroblasts and with sarcoma cells. In cases of doubt, specific staining with Mallory's phosphotungstic acid hematoxylon or Benda's stain for the demonstration of the coarse myoglia fibrils should be applied.

In the variety known as adeno-myoma, endometrial tissue in varying quantity is found scattered throughout the tumor. The endometrial elements participate in menstruation, and sometimes in the areas in which they are extensive, chocolate colored fluid collects in the form of cysts. According to Kelly and Cullen, about 5% of the uterine myomas are adenomatous.

The tumors seem to originate in different ways. Some conform to the requirements of typical tumor growth, beginning as tiny circumscribed points that grow indefinitely; others as more diffused aggregations of the muscular tissue of the organ, and only after considerable growth separate themselves from the parent mass. The latter is particularly true of the adeno-myomas, which Cullen found were usually diffuse in the beginning. Originating somewhere in the thickness of the uterine wall, growth soon brings them either the outer wall, where they become sub-peritoneal, or the inner, where they become sub-mucous. They may arise from the main portion of the body of the uterus, or from the cervix, from one of the cornua or from a Fallopian tube. In many

FIG. 191.—Cystic degeneration of a portion of a pedunculated, subperitoneal myoma (⁵⁄₉ nat. size). The uterus contains numerous nodules. Springing from the right and anterior aspect of the fundus is a subperitoneal pedunculated myoma, 8 × 12 × 14 cm. The upper portion (a) has undergone hyaline degeneration, with subsequent liquefaction. Traversing the cavity everywhere are large and small trabeculæ, dividing the degenerated area into cystic spaces of different sizes. These were filled with a clear, straw-colored fluid. Histologic examination.—The walls of the cystic spaces are composed entirely of hyaline tissue, and there is no endothelial lining. It is interesting to note that the degeneration has occurred at the point farthest removed from the source of blood-supply—the pedicle. Projecting from the surface of the uterus, between the Fallopian tubes, is a small nodule. The upper half is very pale, as indicated by b. The pallor is due to hyaline degeneration occurring in this myoma also. The Fallopian tubes are somewhat thickened. Both fimbriated extremities are free. The tubes were the seat of tuberculosis. The endometrium also showed an early tuberculous process. (*Kelly and Cullen, "Myomata of the Uterus."*)

cases the sub-peritoneal fibroids—myomas—become adherent to the neighbor-
ing structures, omentum, mesentery, abdominal wall, etc., from which they
derive part of their blood supply through newly formed vessels. Under such
conditions, they may grow independently and even become detached so as to
form parasitic tumor masses.

The sub-peritoneal myomas may be sessile or pedunculated, and in the
latter case, may suffer malnutrition through torsion of the pedicle, so that their
substance is subject to degeneration and necrosis. The first stage seems to be

FIG. 192.—An ordinary myomatous uterus on section ($\frac{3}{4}$ nat. size). The uterine cavity
is relatively small and has been encroached upon. Occupying the upper part of the body
are numerous myomata of various sizes and shapes, and with the muscle bundles arranged in
whorls or passing in almost any direction. The myomata stand out in sharp contrast to the
normal muscle, which is much darker in color. (*Kelly and Cullen, "Myomata of the Uterus".*)

hyaline, and appears as focal or widespread areas of whitish or yellowish color
and homogeneous quality. Later this passes into softening, which sometimes
assumes a mucinoid quality, so that larger or smaller areas filled with soft
colorless or yellowish jelly occur. A still more advanced stage furnishes spaces
distinctly circumscribed and filled with more watery fluid. An entire large
tumor may be transformed into one of these cysts, or into a kind of honey-comb
like structure riddled with small cysts.

Sometimes the retrogressive change takes another form, and instead of
softening, the hyaline material calcifies. The salts may be present in small
amounts only, causing the knife to grit a little when the tissue is cut, or in such
enormous quantities as to transform the whole tumor mass into a dense mineral-
ized structure that cannot be cut, but must be sawed in order that its interior
can be inspected. In rare cases bone is formed.

If the tumor becomes sub-mucous, it projects into the uterine cavity which
it dilates. The organ resents this and replies by uterine colic—more or less

rhythmical contractions—which in the long run loosen the attachment of the tumor, which in favorable cases, may be expelled as though a foreign body. Should the expelled tumor be in a state of calcification, and of stony hardness, it would correspond with what were formerly known as "womb stones."

Uterine myomas are commonly multiple, and the entire substance of the uterus may be so riddled with large and small ones as to become an almost unrecognizable nodular mass of irregular shape and size.

Myomas may be very large and Kelly and Cullen have reported one that weighed 89 pounds.

The uterine myomas are commonly supposed to arise through hyperplasia of the uterine muscle, and the fact that they seem, in some cases, to begin more or less diffusely seems to be in favor of that view. Some suppose them to arise from the muscle cells of the blood-vessels of the organ in which they occur. Kelly and Cullen who studied 1307 cases, found the youngest patient to be only 19 years old, the greatest incidence to occur between 28 and 52 and the average age to be 40 years. These ages being the time the patient came under observation, and, of course, not that at which the tumors actually developed.

A third theory supposes the tumors to be derived from myoblasts dislocated from the general mass at the time the Mullerian ducts are forming the body of the uterus and which later take on vegetative activities. Some of those holding this view also suppose that the glandular elements seen in adeno-myoma, are derived from the included tubules of the pronephros. It is not impossible that some of them may have that origin, but, since the participation in menstruation is quite evident in many cases, it seems more probable that they are endo-metrial, and as Cullen seems to think, are "pinched off" at the time the original development of the tumor takes place.

Sampson attributes many adeno-myomas to the accidental implantation of endometrial tissue. He found the so-called *chocolate cysts* of the ovary to result from the collection of menstrual blood in cystic spaces in

FIG. 193.—Adenomyoma of the recto-vaginal septum. (*Cullen.*)

chorista of endometrial tissue in the ovary. The rupture of cysts of such kind, and the escape of their fluid and cellular contents into the peritoneal cavity, where it collects in the posterior peritoneal pouch, is followed by the occurrence of dense adhesions in which are numerous glandular alveoli supposed to be

derived from the distributed endometrial cells. About each of them is the usual cellular endometrial stroma. He supposes that endometrial elements escaping in this, or any other manner, from the ovary, the Fallopian tubes or from the uterus may become implanted in the peritoneal tissue of the uterus, the tubes, or the intestinal wall, where their subsequent multiplication leads to the proliferation of the muscular tissue at the same time that the glands are forming, until adenomyomas result. This origin he believes to be proved by the fact that such tumors not infrequently contain cystic collections of menstrual blood.

The arrangement and distribution of the vessels in uterine myomas are sometimes peculiar and abnormal, and accidents resulting from malnutrition in

FIG. 194.—The line of cleavage between a myoma and the uterine muscle (×55 diam.). *a* is myomatous tissue; *b*, an outer and rough capsule also composed of myomatous tissue; *c* is uterine muscle. At *d* is a definite point of cleavage, the myoma being separated from its outer myomatous capsule by a well-defined space. At *e* the uterine muscle shows a definite inflammatory reaction. (*Kelly and Cullen* "*Myomata of the Uterus.*")

consequence of obstruction, torsion and occlusion are frequent. In some tumors the size and number of the vessels are excessive. Such may be described as telangiectatic, or cavernous. Very vascular tumors are sometimes called *angio-myomas*.

Uterine myomas are distinctly encapsulated, except in the few cases in which their beginnings are diffuse. The capsule is composed of the myometrium, or at least that part of it thrust aside and stretched over the tumor.

In it muscular tissue is present in variable degree, according to the extent of compression and distention to which it has been subjected. The deeper the tumor, the thicker the capsule. The thinnest capsules usually surround the sub-peritoneal growths of considerable size.

Prolonged compression and distention cause more or less of the muscular tissue to disappear by atrophy, so that an old capsule may be almost purely fibrous.

The injury effected by uterine myomas is great. They deform the organ so that conception and pregnancy may be impossible, or having occurred, parturition is impossible. They dislocate the uterus through their weight and occasional attachments to other viscera. They cause uterine colic. They cause
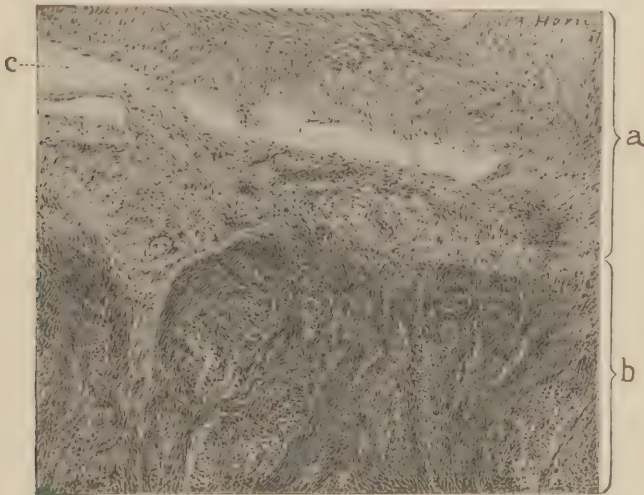
FIG. 195.—Blending of a myoma with the uterine muscle (×100 diam.). *a* is uterine muscle; *b*, very cellular myomatous tissue. The line of junction is very sharply defined, but there is no point of cleavage, the myoma merging directly into the uterine muscle. *c* is a blood-vessel. (*Kelly and Cullen, " Myomata of the Uterus."*)

menorrhagia and metrorrhagia, and postpone the menopause. In addition they are prone to infection, especially the submucous variety, and may lead to the occurrence of abscesses and in some cases to general infection.

Their growth varies in rapidity. Tumors may grow as large as a pregnant uterus at term in two years, or not until after ten. The tumor weighing 98 pounds, to which reference has already been made, was known to have existed for twenty years.

The myoma is a benign tumor. It is, however, advisable to remove it when possible, because of the ill effects mentioned above. Formerly the uterus was always sacrificed for the sake of getting rid of the tumor but of recent years more conservative surgery is practiced, and as the tumors once removed do not come back, the uterus is saved, and its function preserved. Under these circumstances, however, new tumors sometimes appear from beginnings too small

or too deeply situated to be observed at the time of the operation. This is not recurrence, but new tumor development.

In very rare cases myomas seem to be metastatic, and give muscle tumor secondaries. Such are called *myoma malignum*. Many suspect that myomas may "become malignant." Many do show remarkable indication of unusual vegetative activity, accompanied by mitotic figures, and vesicular nuclei, but that any tumor originally benign has certainly become malignant is very difficult to prove. Newton Evans endeavored to find some means of determining by histological examination, the benign or malignant tendency of the unstriped muscle tumors. He was, however, unsuccessful. The only evidence of malignancy seemed to be large numbers of mitotic figures, which, of course really only signified rapid growth.

Myomas of the alimentary canal are next in frequency to the uterine tumors, and may occur in the esophagus, stomach or intestine.

They are usually single, but may be multiple, and in a case reported by Nazzari there were 120. They may be situated below the mucosa—submucous—or beneath the serosa—sub-peritoneal. In most cases they are small, varying from the size of a pea to an almond. In rare cases they grow large enough to cause obstruction of the intestine, and in a few cases to bring about intussusception.

In general macroscopic and microscopic characteristics, they correspond with the uterine fibroids. But they are sometmes more complicated: thus, Cohen observed islands of pancreatic tissue in an intestinal myoma.

Boetticher and Lode divide these tumors into three groups:

1. Small multiple, nodular or polypoid tumors arising from the muscularis, the mucosa being free.
2. Broad thick tumor masses in the muscle layer, to which the mucosa is adherent.
3. Larger sub-serous polypoid tumors that hang in the peritoneal cavity.

Myomas of the skin, the *dermatomyomas*, are supposed to arise either from the *arrectores pilorum*, or from the muscle cells of the vessels.

They usually appear as multiple small nodules, sometimes situated beneath the skin which can be moved over them, or in the skin and moving with it. They are most frequent in the skin of the extremities, buttocks, scrotum and labia. In many cases the differentiation between dermatomyoma and molluscum fibrosum is not easy except by the employment of the specific stains for the demonstration of the myoglia fibrils.

Rhabdomyoma

Rhabdomyoma is a tumor containing striated muscle fibres. It is only with the simple appearing striated muscle tumors that we are concerned here. Whenever a tumor is found to be but partly composed of striated muscle tissue, or to contain it in even small quantity, it should be subjected to the most careful scrutiny to make sure that it is not an embryoma or a mixed tumor, and only after these have been excluded should it be regarded as rhabdomyoma.

There are very few such tumors, but they occur in a wide distribution over the body, usually more or closely in relation with the muscles.

Two varieties seem to occur; that in which the muscle is embryonal in character, and that in which it is adult. The former are usually said to be the more common, but most of them belong in the mixed tumor group. They are composed of spindles, some of which are short, other long, and still others very long and marked by transverse striations. These tumors are certainly related to the sarcomas, and are undoubtedly malignant for the most part. The others are composed in large part of adult muscle fibres, and the striations may be as distinct as in normal muscle of adult type, or difficult to see. The only positive indication that the broad fibres of which the tumor is composed are muscle fibres, may be their staining reaction and the occurrence of the nuclei in parallel arrangement at the edges of the fibres. This adult form of the tumor is, in all probability, benign.

An interesting and rare variety of rhabdomyoma, is found in the heart, where it is usually multiple and congenital. Only about a dozen cases are on record.

The tumor nodes are either buried in the thickness of the cardiac wall or project from the pericardial or endocardial surfaces as soft and edematous pale reddish masses. When subjected to microscopic examination, they are never made up of well-formed and easily recognizable cardiac muscle cells, but of embryonal cells which Mallory describes as rhabdomyoblasts. These cells are not all in the same stage of differentiation, and therefore do not all appear alike. Most of them are quite large, some spherical, some elongated, and some contain several nuclei, while others are vacuolated. The contractile fibres may not appear at all, or be in process of formation and only partly show, or they may be distinct. In addition to a fibrous capsule, not always distinct, the nodes are more or less divided by fibrillar tissue partitions that accompany the blood-vessels into the structure of the tumor.

GLIOMA

A glioma is a tumor composed of neuroglia tissue. Its cells derived from gliablasts, descend from the neuro-ectoderm, and are epiblastic, not mesoblastic. This should be kept in mind when considering the occasional malignant tumors of this class, which are frequently designated gliosarcomas. According to the conventionally adopted view, the sarcoma is a mesoblastic tumor, and malignant gliomas should not be confused with it.

The usual occurrence of gliomas in the central nervous system, commonly results in more or less admixture of nervous elements and raises the question whether it is accidental or essential. It seems to be the former.

Glioma must be carefully differentiated from *gliosis* or *gliomatoids*.

In the following tabulation an attempt is made to indicate the embryogenesis and histogenesis of the tumors of the group.

Neuro-Ectoderm

A. Glioblasts
   (Glioblastoma)
   (Gliosarcoma)

Ependyma
   Ependymal gliosis
   Ependymal glioma
      Contains gland-like spaces.
      Cells contain cytoplasmic
         rods and granules

Neuroglia

B. Neuroblasts

Gliosis—Inflammatory
         Regenerative
         Syringomyelia
         Sclerosis cerebri diffusa

Glioma
   Astrocytoma
   Glioma molle
   Glioma durum

C. Sympathoblasts

Clinical varieties
   Cerebral
      Cortical
      Pial
      Central
      Ependymal
   Spinal
      Superficial
      Central
   Peripheral
      Retinal
      Nasal
      Coccygeal

Gliomas may arise wherever neuroglia tissue normally occurs, in the brain, the spinal cord, and the retina, as well as where it occasionally or abnormally occurs, as at the anterior and posterior ends of the cerebro-spinal axis (neural canal) at the nose and at the coccyx. But when tumors resembling glioma occur in connection with the peripheral nerves and sympathetic systems, they may be suspected to belong to one of the related groups of tumors and to arise from neuroblasts or sympathoblasts.

The glioma is so varied that it is extremely difficult to describe either grossly or microscopically. For example, in a certain number of cases it appears as a distinct, well circumscribed, rounded or nodular, grayish or grayish-red, firm mass, embedded in the nervous tissue from which it is well separated, though it is probably never encapsulated. In other cases it occurs in the form of a soft, dark-red, hemorrhagic, elevated or depressed area that fades away on all sides into the brain tissue. The former looks like a tumor, the latter more like an area of red softening or hemorrhage. These differences are found, however, to depend upon variation in the vascularity of the tumor and upon the healthy or degenerated condition of its tissue rather than upon essential difference in its structure, though sometimes the density of the tumor tissue is increased through the addition of fibroblastic elements from the pia, which give it firmness. Hemorrhage, mucoid degeneration, necrosis, fatty degeneration, calcification, and cyst formation, all play a part in complicating the gross morbid picture as well as the microscopy. Thus are explained the differences between *glioma durum*, *glioma molle*, *glioma cysticum* and *glioma apoplecticum*.

Gliomas are usually solitary, but may be multiple. They may arise in any part of the brain—cerebrum, cerebellum, pons or medulla—and may be embedded or project externally or into the ventricular cavity. They usually grow slowly, but may grow rapidly. The symptology varies according to the position occupied, but they usually have in common increased intra-cranial pressure, choked disc, elevated blood pressure, and occasional apoplectic attacks. When superficially situated and circumscribed they may be operable.

FIG. 196.—Glioma of the retina. (*From a patient of Dr. L. Webster Fox, in the Medico-Chirurgical Hospital, Philadelphia.*)

The tumors are benign in the sense that they do not occasion metastasis, but they are locally extremely destructive through pressure, invasion of new tissue and hemorrhage, and are usually fatal. The more infiltrative varieties occasionally invade the pia, but seem never to pierce it. If successfully removed the intracranial tumors seem not to return, but the extra-cranial ones return again and again, attain to an immense size, ulcerate, and cause death through hemorrhage and infection.

The cells of the normal neuroglia vary greatly in size and shape, some are rounded, others irregular or spindle shaped and only a few of them are distinct astrocytes. The fibrils are in intimate contact with the cells and run from them in two directions. According to Mallory they "do not start from the cells, but

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course along the surface of the cytoplasm with which they are in intimate contact, and extend away from the cell in two directions. Every cell is surrounded by perhaps one or two dozen fibrils of undetermined length. Around the spherical cells they run in all directions; around the spindle-shaped cells they run parallel to the long axis of each."

In glioma the neurogliar structure is repeated with variations and modifications that seem to depend in part upon the rapidity of growth. Rapidly growing tumors may be almost purely cellular, slowly growing ones largely fibrillar,

Fig. 197.—Glioma of the pons Varolii. The pale area is the tumor. (*From a specimen in the Pathological Museum of the University of Pennsylvania.*)

and the fibrillae may be fine or coarse in different cases. Admixture of connective tissue from the pia sometimes gives them an alveolar appearance. All infiltrating gliomas show a considerable number of nerve cells at the periphery, derived from the nervous structures into which the tumor is growing, but which soon perish as the tumor extends. They are nearly always highly vascular usually more or less hemorrhagic, and commonly more or less degenerated.

The extra-cranial gliomas differ in various particulars. The glioma retinae may arise from the ciliary or posterior portion of the retina. It at first appears soft and bluish, but soon become milky, grayish or yellowish from associated fatty degeneration and calcification, or turns red from hemorrhage, or soft from degeneration and necrosis. It may be single or multiple, and in the latter case, may occur simultaneously or consecutively in both eyes. The retina soon becomes stripped from the choroid which becomes invaded. In the mean time, the cavity of the vitreous becomes filled, and the tumor begins to travel along the optic nerve toward the brain. If the globe of the eye be removed, the

tumor returns in the orbit which it soon fills, recurring again and again when removed, and finally projecting externally in the form of a fungous mass which is hemorrhagic, ulcerated, and becomes infected, so that the death of the patient is brought about if the intra-cranial development does not previously destroy him.   In some cases no recurrence was noted after the enucleation of the eyeball.   In a few cases the tumor gave metastasis to the brain, spinal cord, meninges, lymph-nodes and internal organs.

The microscopic structure of these tumors is somewhat different from those occurring in the brain.   Many are almost uniformly composed of small round cells resembling lymphocytes, in that they have large nuclei and scarcely any cytoplasm.   There are no astrocytes, and in many cases no fibrillae.   Such
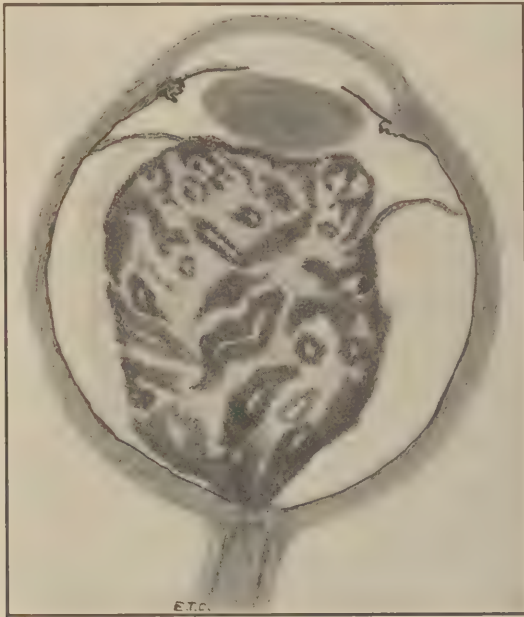
FIG. 198.—Section through an eye containing a glioma of the retina.   The growth is mainly from the outer surface of the membrane—"glioma exophytum." The characteristic patchy way in which it stains due to areas of degeneration, is shown.   (*Collins and Mayer.*)

tumors are apt to be called small round cell sarcomas, or glio-sarcomas, but the clinical course without metastases is differential, even were the point of origin not sufficient.

In not a few cases the cells are arranged about the blood-vessels in the form of perivascular cylinders—an appearance probably caused by the wide-spread degeneration of the cells rather than because of any essentially different structure.   Such tumors are frequently mistaken for, and called peritheliomas, perithelial sarcomas or endotheliomas.

But the most striking, characteristic, and diagnostic appearance of the extra-cranial gliomas is the presence of tiny rosettes in the cellular portions.   These consist of a row of cuboidal or semi-columnar cells arranged about a central

opening, and thus bear a partial resemblance to an acinus of an epithelial gland. When the lumina are distinct and limited internally by a membrane, blunt or pointed protoplasmic prolongations resembling cilia sometimes project into the lumen.
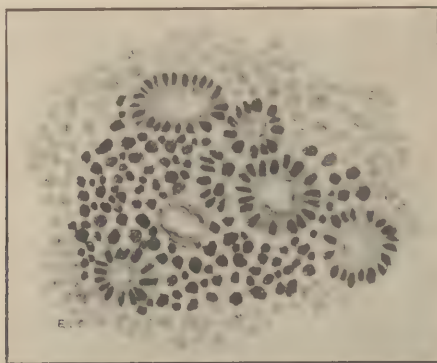
FIG. 199.—Semi-diagrammatic drawing of a microscopic section of a glioma of the retina showing the rosettes.   (*Collins and Mayer.*)

Flexner was one of the first to observe these, and interpreted them to indicate the presence of neuro-epithelial cells, and the rosettes as abortive attempts at the formation of a retina.   The cells of the rosettes closely resemble

FIG. 200.—Microscopic section of a glioma of the retina.   The dark parts are well-preserved, the pale parts necrotic.   Throughout the former are great numbers of tiny dark circles which are the characteristic "rosettes."   (*Photomicrograph by Prof. Allen J. Smith.*)

epithelium, the delicate membrane lining the space can be considered as the equivalent of the internal limiting membrane, and the projection of the cells beyond it as corresponding to the layer of rods and cones.   On this account he called it *neuro-epithelioma.*

But tumors with simple rosettes, and others with these more complicated rosette-like structures may or may not be different things; they seem to merge

into one another, and what is most interesting, similar tumors with rosette formations have been observed at the coccyx. The absence of any retina forming tissue in that distribution has caused some pathologists to cease to regard these tumors as having anything to do with the retina, or to be derived from it. but look upon them as Mallory does, as neuroblastomas, in which a few neuroblasts have, by chance, become incorporated.

Gliomas supposed to be derived from displaced vestiges of the neural canal, and appearing at the nose and coccyx are extremely rare. They do not resemble the more frequent forms of glioma, but simulate other tumors. Thus, one such tumor reported by Mallory looked very much like carcinoma, because its cells had insinuated themselves between the separated fibres of the connective tissue. To determine the true nature of such a tumor, it may be necessary to apply the specific stains already referred to. Even when this is done, the interpretation should be guarded as the difference in the color reactions between the fibrils of fibrin, fibroglia and neuroglia are slight.

The gliomas of the adrenal body, and sympathetic ganglia are not gliomas, but belong in some one of the groups next to be described.

GLIOSIS

Gliosis is hyperplasia of the neuroglia. It sometimes occurs with fair circumscription, and is always difficult to differentiate from glioma, on account of the indefinite circumscription so common in that peculiar tumor. Gliosis most commonly follows degenerative disturbance of the central nervous system, and is usually thought of as comparable to the hyperplasia of fibrillar connective tissues. It is characterized by cell proliferation with exaggerated fibril formation, the fibrillae sometimes being condensed by pressure and collapse so that the substance is quite firm. The newly formed neuroglia seems to be of low vitality, and prone to degeneration and cyst formation. The condition known as *syringomyelia*, is characterized by gliosis with subsequent degeneration and cyst formation. Some neuro-pathologists look upon it as a tumor, others as simple gliosis following primary degenerative change in the gray matter of the spinal cord.

NEUROMA

A neuroma is a tumor composed of nervous tissue.

In his "Textbook of Pathology," MacCallum makes the following important preliminary statement:

"Originally the epiblastic cells which line the medullary groove are capable of developing into nervous elements or into supporting glial cells The production of the peripheral nervous system is due to the outgrowth of new fibres from the central region but in addition to this, many of the neuro-epithelial cells wander into the interior of the body and assume certain positions in relation to the organs where they give rise to the cells and fibres of the sympathetic system. Their invasion into the interior of the rudiments of the adrenal glands results in the formation of the medulla of those glands in close relationship to the adjacent sympathetic ganglia. Similar modification of some of those invading neurocytes in other situations lead to the formation of the analogous chromaffine bodies which are found in close relation with the

sympathetic ganglia in the thorax and retroperitoneal tract. It is necessary to believe that these cells may also give rise to the less specialized attendant or supporting cells in each of these situations."

It is also necessary to bear in mind that inasmuch as a nerve fibre is but a greatly prolonged process of a nerve cell, it is inconceivable that there should exist nerve fibres independently of nerve cells.

In the following tabulation, which is a continuation of that with which the section upon glioma began, the relation of the various tumors included under the general heading neuroma is shown.

Neuro-ectoderm

A. *Neuroblasts*
  Neuroblastoma
  Adrenal
  Brain
  Lung

  (a) Nerve cell tumor.
    Neurocytoma. Marchand's case of little tumor of the Gasserian ganglion.
  (b) Nerve fibre tumor.
    Neurinoma.
    Cerebral.
    Spinal.
    Peripheral.

  1. True neuroma
    Plexiform
    Traumatic— amputation neuroma.
  2. False Neuroma.
    Neuro-fibroma.
    Neuro-fibroma molluscum.

B. *Sympathoblasts*
  Sympathoblastoma
    1. (J. H. Wright's "Neuroblastoma of the adrenals of children, of the retroperitoneum a n d pelvis, with rosettes of cells).
    2. (Martin's single case of tumor of the neck with cells supposed to be in transition between neuroblasts and ganglion cells).

  (a) Sympathetic ganglion cells.
    Neuroma ganglionare.
    Retro-cervical.
    Retro-peritoneal.
    Pelvic.
  (b) Peripheral glia cells.
    Glioma of the adrenal.
  (c) Chromaffine cells.
    Paraganglioma.
    Usually occur in the medulla of the adrenals of old people. The cells are too young to give the brown color with chromium salts. No tumors of true Phaechromocytes are known.

The false neuroma has already been considered in the section upon fibroma, but it seems necessary to add a little to what has been said. These are fibrous or myxoid tumors of single or multiple occurrence along the course of the nerves, sometimes attaining the size of a goose egg. Considerable lengths of a nerve, and its branches may be studded with them. Attempts have been made to show that although the greater part of the tumor is composed of the fibrillar connective tissue, yet there is an increase in the number of nerve fibres. How could there be? Where could they come from? The growth of the fibrillar or other connective tissue in the nerve might cause elongation and inequality

of the nerve fibres, but that it should cause increase in their number seems to be impossible when it is recalled that a nerve fibre is but the prolongation of a nerve cell process.

A peculiar variety of false neuroma is the *plexiform* or *cirsoid* neuroma, which sometimes occurs upon the face, eye-lid, neck, breast, and back. It appears to be some kind of developmental defect by which an excess of perinurium and endonurium of the nerve concerned causes it to become transformed into an elongated nodular swollen structure easily palpable beneath the skin, and described as feeling like a "bunch of worms." There seems to be very little functional disturbance of the nerves as the fibrillar tissue upon which the enlargement depends seems to be too soft to effect damage through pressure.

Ever since the time of Virchow it has been the custom to divide neuromas into the fibrillar and ganglionic forms, and though there are now valid objections to it, it will be followed here, not because it is scientifically accurate, but because it is convenient.

I. *Fibrillar Neuroma—Neurinoma.*

Two varieties are described:

Neuroma myelinicum, occurring in connection with the medullated nerves, and

Neuroma amyelinicum occurring in connection with the non-medullated nerves of the sympathetic system.

The *amputation neuroma* is a pyriform enlargement that frequently appears at the ends of severed nerves, especially those of amputated limbs, and sometimes causes great suffering when sensory fibres are caught in and compressed by scar tissue. It is not a true tumor. When a nerve is severed, the distal part degenerates, and function ceases. But in the course of time regeneration occurs through the downward growth of the proximal ends of the axis cylinders which may eventually connect with the peripheral nerve ending and reestablish function. But in an amputated limb, there are no peripheral nerve endings, and in widely separated fragments it may be impossible to bridge the interval, when the growing and separated regenerating fibres are compelled to terminate in a mass of fibroblastic tissue, forming the tumor-like enlargement.

II. *Ganglionic Neuromas.*—These tumors form masses consisting of both nerve cells and fibres.

How do these tumors grow? So far as is known there can be no multiplication of mature differentiated nerve cells, yet the nerve cells in ganglionic neuromas must multiply, for immense numbers of them appear, and many mitotic figures can usually be found. There is, then, a striking difference between the behavior of the tumor cells and the normal cells. There is also a difference in appearance. The cells from which the tumor is actually growing seem to be embryonal, undifferentiated, and vegetative. They may differentiate subsequently, and send out the processes that become the nerve fibres, but it is from the still undifferentiated cells that the growth of the tumor takes place. The primordium of the tumor may, therefore, be looked upon as a primitive embryonal nerve cell—a neuroblast or sympathoblast. It would be desirable to improve the nomenclature of these tumors by calling those

derived from the neuroblasts, neuroblastomas; those from the sympathoblasts, sympathoblastomas, and those from the phaechromacytes, or chromaffin cells, phaechromocytomas. But the tumors are so rare, and have been so little studied with such object in view, that it is not possible to do so in the present state of knowledge. As the matter stands at present, the following have been described, and seem to represent an ascending scale in the steps of nervous tissue development. The neuro-epithelioma is not included as it was discussed under the heading Glioma.

Neurocytoma.—Under this name Marchand described a tumor that he supposed to be derived from the undifferentiated cells of the neuro-ectoderm, and to represent the most primitive type of nervous tissue tumor. It grew in the Gasserian ganglion, and was composed of small round cells of lymphoid appearance, with fine fibrillae forming the ground work. It must be difficult to make a microscopic diagnosis of such a tumor, but as, thus far, very few additional cases have been reported it not likely to be a frequent source of perplexity.

Neuroblastoma.—Here one sees the confusion that may result from the lack of consensus of opinion in nomenclature. Mallory uses neuroblastoma for all tumors arising from nerve cells, but J. H. Wright, who seems to have been the first to employ it, restricts it to a variety of tumor that he observed in infants, children, and, very rarely, in young adults, and which is characterized by a histologic structure much like glioma.

It usually occurs in the adrenal, but may occur in the sympathetic plexuses behind the peritoneum. Its high degree of malignancy and disposition to early metastasis usually destroy the patient before growth to a large size is possible.

When microscopically examined the tumor is found to be composed of small rounded cells with scanty cytoplasm, and an intermediate fine fibrillar stroma. Rosette formation such as occurs in glioma is common, and might lead to the diagnosis of glioma were it not for the fact that the fibrillae arising from the cellular prolongations and generally pervading the substance of the tumor fail to give the specific staining reaction of neuroglia. Wright believes the tumor to originate from the sympathetic formative cells, which he calls "sympathogonia"—(sympathoblasts?).

Sympathoblastoma.—Martius studied a tumor of the neck that seemed to be composed of nerve cells in various stages of development, from undifferentiated round cells to ganglionic cells of which there were a good many. He looked upon it as composed of tissue representing the transition stage between the neuroblasts and ganglion cells of the sympathetic system. No other tumor of exactly the same structure seems to have been observed.

Ganglion Neuroma.—This tumor usually occurs in children, and arises in the retro-peritoneal, cervical or pelvic regions, apparently from structures connected with the sympathetic nervous system. It grows slowly, forming a rounded, nodular, more or less circumscribed mass, of pale color, and fibrillar appearance.

When examined histologically, it is found to be composed of nerve cells and fibres, in a more or less well differentiated condition.

The fully formed nerve cells do not differ appreciably from those of the sympathetic system—ganglionic cells—and occur in groups in the midst of a

fibrillar matrix consisting of bundles of non-medullated nerve fibres winding their wavy course this way and that through a delicate connective tissue with numerous blood-vessels.

One such tumor was brought to the author by Dr. F. J. Hammond of the State Asylum for the Insane at Trenton, N. J. It had been removed by a Trenton surgeon, from the abdomen of a little girl of twelve years, who had known of its presence only for three months, although the tumor weighed four and a half pounds. Histologically, it consisted of bundles of imperfectly formed wavy nerve fibres, in a very soft matrix of fibrillar connective tissue, with numerous scattered aggregations of large well formed ganglionic nerve cells. Here and
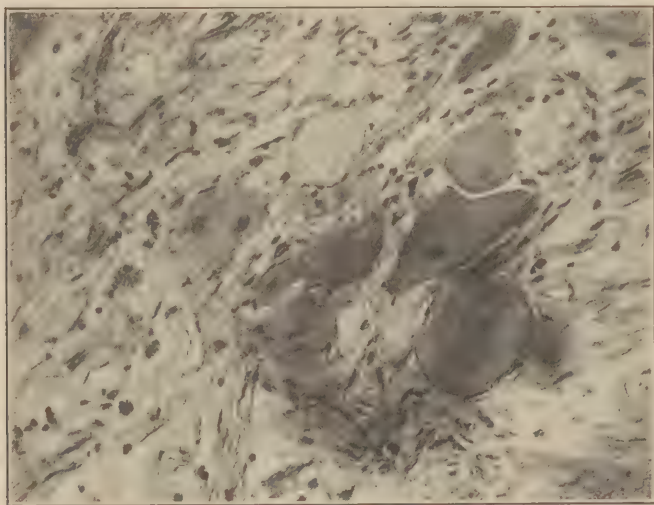
Fig. 201.—Microscopic section of a ganglion neuroma. The tumor is that mentioned in the text as occurring in the abdominal cavity of a young girl. (*Photomicrograph by Prof. Allen J. Smith.*).

there were other groups of nerve cells less well formed, together with some small, presumably very young, cells. Some of the less well differentiated cells had two, and in one case three nuclei, and some irregular karyokinetic figures were found. The subsequent history of the patient is unknown. Such tumors ought to prove benign, though Benecke observed an apparently similar case in which metastasis occurred.

Paraganglioma.—A few rare tumors of the medulla of the adrenal gland have been observed to consist of cells that colored brown with chromium salts. They are supposed to arise from the formative cells of the sympathetic nervous system —sympathoblasts—in a fairly well-developed stage of evolution. They seem to occur only in adults, and are benign in disposition. Beitzke found such tumors in the carotid gland, and described them under the name *Struma intercarotica.* Simmons called them Paraganglioma intercaroticum.

LYMPHOMA

Upon theoretical grounds, a lymphoma should be a tumor derived from lymphoblasts, composed of lymphocytes, and benign in disposition, but it is doubtful whether there is any such tumor. There are, however, many tumor-like enlargements of diverse nature, to which the name lymphoma has from time to time been applied, with the result that bewildering confusion attends all tumors that have to do with the lymphoid tissues or the lymph nodes.

The following tabulation affords a convenient starting point for the consideration of such facts about the lymphatic tumors and tumor-like growths as are available:

    I. Lymphoid Hyperplasia Associated with Systemic Disease.
       A. Chiefly Affecting the Lymph-Nodes.
         (a) Accompanied by altered relationship of the cellular components of the blood.
            Lymphatic Leukemia.
         (b) Unaccompanied by altered relationship of the cellular components of the blood.
            Aleukemic Leukemia, (the *Pseudoleukemia* of Cohnheim).
       B. Chiefly Affecting the Bone-marrow.
         (a) Accompanied by definite cellular changes in the blood, and commonly by associated changes in the spleen.
            Myelogenous Leukemia.
         (b) Unaccompanied by definite cellular changes in the blood.
            1. Resulting chiefly from multiplication of myelocytes.
               Multiple Myeloma.
            2. Resulting chiefly from multiplication of plasmacytes.
               Plasmacytoma.
            3. Characterized by green color of the freshly cut surface.
               Chloroma.
   II. Lymphoid Hyperplasia Independent of Systemic Disease.
       A. Arising in the Lymph-nodes.
         (a) Resulting from infection of known nature.
             Tuberculosis.
          (b) Resulting from infection of unknown nature.
             Lymphogranuloma:—
               Hodgkin's disease.
                Paltauf-Sternberg infection.
                Fraenkel-Much infection.
                Bunting-Yates infection.
       B. Arising Apart from the Lymph-nodes.
         (a) In the Lachrymal and Salivary glands.
             Mikulicz's Disease.
         (b) In the Skin and Subcutaneous Tissues.
             Granuloma (Mycosis) Fungoides.
  III. Tumors Arising from Lymphoid Tissue.
       A. Benign.
        Lymphoma.
       B. Malignant.
        Lympho-sarcoma.

LYMPHATIC LEUKEMIA

The enlarged lymph-nodes that form the usual early manifestations of leukemia are in certain respects like tumors. They consist of circumscribed nodes, and though each, through its position and relations, can be recognized as a

lymphatic node, its histological structure is changed through the disappearance of the germinal centers, and the closing of its sinuses so that it presents a remarkably uniform appearance. But these enlargements differ from tumors in being part of a systemic disease accompanied by changes in the blood.

It seems to be the "latest fashion" to speak of the leukemic conditions as tumors, but to do so is inconsistent with the general conception of tumor as defined in our opening section.

Simultaneous enlargement of lymph-nodes in different regions of the body does not impress us as suggesting tumor, nor does simultaneous diffuse hyperplasia of the marrow of many bones, such as occurs in the myelogenous form of the disease, resemble tumor in any ordinary sense.

With respect to the aleukemic form of leukemia, in which the nodes enlarge simultaneously or consecutively without indication of systemic disease, our attitude is the same. They are multiple, hyperplastic, depend upon what appears to be the same stimulus, and in many cases later becomes leukemic.

Multiple Myeloma

A closer resemblance to tumor is seen in multiple myeloma. It is characterized by the multiple occurrence of soft reddish nodes that arise from the marrow of the ribs, vertebrae and cranium, rarely from other bones. Histologically there are four recognized types of structure (1) plasmacytoma; (2) lymphocytoma; (3) myelocytoma, and (4) erythroblastoma. The cells of any one of these varieties multiply in the marrow spaces, cause atrophy of the delicate partitions of the spongy structure, until masses of considerable size are formed. They frequently grow in the shaft of a bone filling the marrow cavity. The outer dense bone is then cleanly penetrated, and the tumor projects into the softer tissues as a soft, rounded, reddish node of fairly uniform texture. They occasionally cause changes in the regional lymph-nodes, and may be metastatic. But as one inquires further, it is found that the nodular formations are not the whole story, for the patient also suffers from certain constitutional symptoms, among which is the appearance of a peculiar protein, the Bence-Jones protein, in the urine and an increasing weakness such as appears in leukemia. Moreover, the patient commonly succumbs in the course of five or six years without enough local disturbance to account for his death, and without metastasis of the tumor.

Chloroma

Even more like a tumor, and almost always classed as such, is the chloroma, or green tumor, so called because section of its fresh tissue shows a bright green color. In most cases it arises from the bones of the cranium, but occasionally occurs in the soft tissues, such as the breast. It is a soft, circumscribed but unencapsulated node, histologically composed of myeloid or lymphoid cells, in and among which is distributed an unknown pigment—probably a lipoid— which gives it the green color. But upon examining the reported cases of this lesion, it is found that it is not uncommonly multiple, and that in nearly every

case the appearance of the tumors has been either preceded or followed by leukemic changes in the blood. It is therefore probable that the chloroma is but another manifestation of constitutional disease, and not a real tumor.

HODGKIN'S DISEASE

A second group of lymphatic enlargements must be separated from tumors because of the probability that it is an infectious disease.

FIG. 202.—Young man 18 years of age with typical deformity resulting from the enlargement of the cervical glands in Hodgkin's disease. The patient died 4 months after this photograph was taken, and 8 months from the beginning of recognized illness. (*Longcope.*)

The first upon the list is tuberculous adenitis, which was always considered to be a form of lymphoma until its infectious nature was shown by the histological agreement of its lesions with tuberculosis in general, and by the presence of tubercle bacilli. But this only applies to the typical cases, and it is by no means always certain what is and what is not tuberculosis in the lymph-nodes. Next

comes Hodgkin's disease, described by Hodgkins in 1832, and named after him by Bennet. It is a disease most frequent in men, in the third decade of life, and characterized by the unexplained enlargement of the lymphatic nodes, the order of frequency being the cervical, axillary, inguinal, retro-peritoneal and mediastinal.

FIG. 203.—Cervical, submental, mediastinal, branchial, retroperitoneal and left axillary tumors from the case shown in the portrait. The tongue is visible at the top of the picture in the middle line. A short distance below is the thyroid gland. The left axillary tumors are attached to the mass of cervical glands on the left side. (*Longcope.*)

Sometimes the enlargements remain confined to the region in which they began, more frequently they spread to others, and sometimes they are accompanied by lesions of the internal organs, having identical structure.

These enlarged nodes are at first soft, and were doubtless included among what were formerly known as *soft lymphomas*. But as time passes, they become

harder, and then form part of what were formerly known as *hard lymphomas*. Progressive enlargement with invasion of the surrounding structures and occasional metastasis has caused some cases to be described as *malignant lymphomas*.

Enlarged single nodes can usually be excised with ease. When a whole system is involved, the affected nodes usually remain discrete, or are bound together by a common surrounding connective tissue sheath that can be easily and cleanly dissected out. Only very late in the disease are there infiltrating extensions or connections.
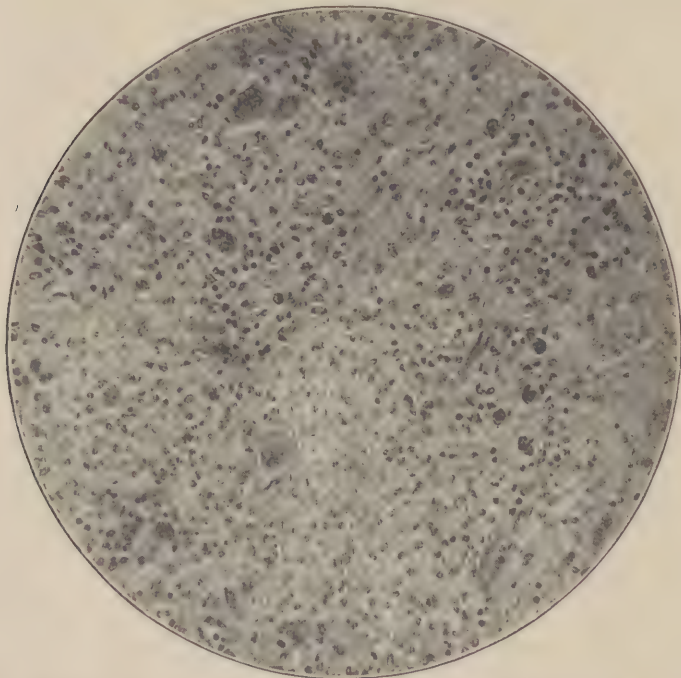
Fig. 204.—Microscopic section of a lymph-node of Hodgkin's disease, showing the disappearance of the normal structures, and replacement by fibroblasts, plasma cells, eosinophiles, and the small giant cells. The lesion is old enough for the fibrous stroma to be distinct. (*Photomicrograph by Prof. Allen J. Smith.*)

When the cut surfaces are inspected, young lesions are uniformly pinkish gray but older ones may be partly necrotic, and marked by yellowish patches, or hemorrhagic, and marked by red or yellow brown (from the presence of hemosiderin), and very old ones may be divided by bands of fibrillar connective tissue, or be distinctly fibroid.

When the nodes are examined histologically, an equally varied picture is observed. The younger lesions are almost entirely cellular; older ones partly fibrillar. The younger lesions are composed of cells of diverse orders, the greater number being lymphocytes, probably antecedent in the affected node. In older lesions these seem to be gradually replaced by an increasing number of larger cells of epithelioid type supposed by Reed to be derived from the reticulum cells. Whatever their origin, their appearance soon completely

destroys the architecture of the node, and all trace of lymph nodules, cords and sinuses disappear.

But, in no case is the cellular structure uniform; it is composed of lymphocytes, epithelioid cells, plasma cells, and eosinophil cells in varying proportions, and among them lie numerous fibroblasts, and what is esteemed of diagnostic importance, many peculiar small giant cells, now frequently spoken of as "Dorothy Reed giant cells" after the observer who first regarded them as impor-
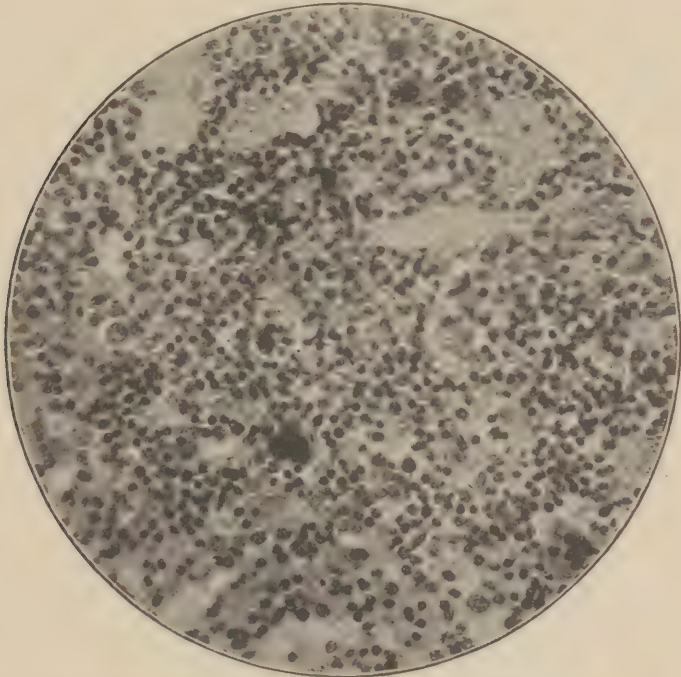
FIG. 205.—Higher magnification of a part of the same section shown in the preceding illustration, enabling the cells to be better examined. (*Photomicrograph by Prof. Allen J. Smith.*)

tant. These giant cells are very different from those seen in ordinary tuberculosis—the cells of Langhans—being much smaller in size, having proportionally very much larger nuclei, usually not more than three or four, crowded together in the center of the cell. The number of these giant cells varies. In some cases they are very few, in others numerous, and in some parts of the same section there are more than in others. The shape of the giant cells also varies; the smaller ones are usually distinct in outline, the larger have peripheral protoplasmic prolongations. What seem to be intermediate stages between epithelioid and giant cells can be found, and it seems probable that they arise through some modification in the reproduction of the latter. In rare instances typical cells of Langhans may be found, but they are so rare as to be regarded as accidental and of no significance in making the diagnosis.

In the older lesions the structure is modified by bands of fibrillar tissue, growing from the capsule and penetrating deeper and deeper into the structure.

Their formation is foreshadowed by the appearance of an increasing number of fibroblasts.

As the disease extends, and an ever increasing number of lymph-nodes is involved, nodular tumors, having identical cellular structure, appear in the spleen, the lungs, and sometimes in the bone marrow. In rare instances such tumors seem to appear in the internal organs independently of preceding disease of the lymph-nodes. These are difficult to understand, and may not be Hodgkin's disease but some real tumor.

As to the nature of the lesions there is no consensus of opinion. The structure suggests granulation tissue rather than tumor and on this account an increasing usage has been made of the term *lymphogranuloma* in describing it. Sternberg is of the opinion that it is a manifestation of tuberculosis, some variation in the virulence of the bacilli possibly explaining its unusual histological features. Fraenkel and Much also look upon it as a manifestation of tuberculosis, and believe that they have fully accounted for it by a peculiarity of the bacillus, which is said to lack its customary "acid-fast" quality. By carefully staining sections by Gram's method, they have demonstrated rows of fine granules which they interpret to be tubercle bacilli in this unusual form. One might suppose that the question could easily be settled by the implantation of some of the affected tissue into guinea-pigs, which ought to develop tuberculosis if these granules are, indeed, tubercle bacilli. But in this respect results differ. The material from some cases is said to have produced tuberculosis in the experiment animals, but usually it does not.

Bunting and Yates believe that certain diphtheroid bacilli, found by them, are the cause of the disease. These, however, have not been found in all cases. Kofoid, Boyers and Swezy believe that they have demonstrated Endameba dysenteriae in the lesions of Hodgkin's disease, which may be a form of amebiasis.

The successive claims made for these various micro-organisms remind one strongly of the history of the pursuit of the cause of cancer.

Hodgkin's disease is steadily progressive. If the affected lymph nodes are excised, others soon show enlargement. If some disappear under the influence of X-rays, the same may usually be expected, though some cases are said to have completely recovered when thus treated. The affected nodes enlarge to greater and greater size until they mechanically erode the bones (sternum, ribs, vertebrae) or obstruct or compress important viscera (trachea and bronchi) to an extent that compromises life. Not infrequently the enlarged nodes break bounds and instead of remaining confined by the surrounding sheath of connective tissue, infiltrate and metastasize to central organs. Such cases are usually supposed to have become sarcoma, and Hodgkin's sarcoma is recognized by some as a distinct entity.

As the end approaches, the patient suffers from constitutional symptoms, in the form of secondary anemia, depression and cachexia or general malnutrition, with bronzing of the skin, pruritis, dermatitis and fever. Nearly all cases are fatal, acute cases in a few months, chronic cases after a few years.

On account of the clinical resemblance the early stage of the disease bears to lymphatic leukemia, it was formerly frequently known as *pseudoleukemia*. That is, however, a misnomer.

Pseudoleukemia is a distinct entity, first described by Cohnheim, as an enlargement of the lymph-nodes without the lymphocythemia of leukemia. What he described undoubtedly corresponds to what is now recognized as the aleukemic form of lymphatic leukemia, and is not the lymphogranuloma.

Mikulicz's Disease

This rare affection is chiefly characterized by a lymphoid hyperplasia that makes its appearance in the stroma of the lacrymal glands, eye-lids, lips, and

Fig. 206.—Mikulicz's disease. (*Fisher.*)

salivary glands. The enlargement of the parts results in a very peculiar, grotesque and characteristic expression of the face. Its etiology is unknown. Some cases have been associated with leukemia, others not. It would not be mentioned here were it not that some believe it to be a manifestation of leukemia, and leukemia a manifestation of tumor.

Granuloma Fungoides, Mycosis Fungoides

Another disease sometimes considered to be a tumor, but apparently without justification, is *granuloma fungoides*. Occasional patients have been or become leukemic, on which account a few authors incline to view it as a manifestation of that disease. But the blood disturbance of leukemia is not to be found

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in true granuloma fungoides. There may be marked eosinophilia, but there is no lymphocytosis worth mentioning. The leukemia theory may be the result of confusing with granuloma fungoides the occasional lymphoid deposits that make their appearance in the skin of leukemic patients.

The lesions of this disease occur in the skin, chiefly of the upper half of the body, may be single or multiple, and vary in size up to a tangerine orange. A woman of middle age suffering from the disease, who came under observation in the Philadelphia General Hospital had two lesions only, one upon the left side of the forehead, the other upon the dorsal aspect of the right wrist. The latter lesion was perfect, that is, not ulcerated. It was about the size of a small tomato which it very closely resembled in color and shape, as well as in the peculiar, shining, thin, translucent quality of the cuticle by which it was covered, and by its softness. While the patient was in the hospital it became injured and infected, and the greater part of its sloughed away, leaving a large indolent ulcer. What became of this patient is not known. In many cases the ulceration is followed by cicatrization, but as the older lesions heal, new ones develop, so that there is always more or less open surface to admit infectious agents, to whose effects the patients usually finally succumb.

When the lesions are histologically examined there is little resemblance to tumor. The tissue is a vascular granulation tissue in which are found all the miscellaneous cells by which it is usually characterized—lymphocytes, eosinophils, mast cells, plasma cells, fibroblasts, epithelioid cells, giant cells such as occur in Hodgkin's disease and, in cases with open lesions and infection, foreign body giant cells.

Some have considered granuloma fungoides to be a form of sarcoma of the skin, but from their descriptions of the histology of the lesions, it seems as though sarcoma of the skin may have been mistaken for granuloma fungoides.

LYMPHOMA—LYMPHADENOMA

Lymphoma seems to be an obsolete term at present.

Lymphadenoma usually means enlargement of a single lymph-node. If histological examination shows an enlargement without essential alteration of structure, the condition is hypertrophy and not tumor; if the structure be modified, the enlargement will, as a rule, be found either to be inflammatory or to fall into one of the classes already described.

LYMPHO-SARCOMA

This is a highly malignant tumor arising from the lymphoid tissues, hence frequently from the hymph-nodes, composed of lymphocytes, and characterized by rapid growth, infiltration of the surrounding structures, and early metastasis through the blood. It is identical with what is commonly described in the text-books as small round cell sarcoma, which will be more fully considered in the following section.

MALIGNANT TUMORS
SARCOMA

A *Sarcoma* is a malignant tumor of mesoblastic derivation, chiefly composed of rapidly multiplying cells resembling those of the connective tissues. It presents itself in many different forms as shown in the following tabulation:

I. Tumors of mesenchymatous derivation—true sarcomas.
  A. Simple sarcomas
    1. Round cell sarcoma
      (a) Small round cell sarcoma
        Lympho-sarcoma
      (b) Large round cell sarcoma
    2. Spindle cell sarcoma
      (a) Oat-shaped cell sarcoma
      (b) Small spindle cell sarcoma
      (c) Large spindle cell sarcoma
      (d) Irregular cell sarcoma

    3. Giant cell sarcoma

                Pseudosarcoma gigantocellulare
                  —benign giant cell sarcoma
                Sarcoma gigantocellulare—
                  malignant giant cell sarcoma

  B. Complex sarcomas—containing more or less admixture of adult connective tissues, but behaving like sarcoma clinically.

COMMON NAMES	PREFERRED NAMES
Fibro-sarcoma	Fibroma sarcomatodes
Myxo-sarcoma	Mxoma sarcomatodes
Lipo-sarcoma	Lipoma sarcomatodes
Chondro-sarcoma	Chondroma sarcomatodes
Osteo-sarcoma	
Osteoid sarcoma	
Osteo-chondro-sarcoma	Osteoma sarcomatodes
Ossifying sarcoma	
Leiomyo-sarcoma	Leiomyoma sarcomatodes
Rhabdomyo-sarcoma	Rhabdomyoma sarcomatodes
Angio-sarcoma	Angioma sarcomatodes

II. Tumors of ectodermal derivation confused with sarcoma.

Neuro-sarcoma (malignant neuroma)	Neuroma sarcomatodes
Glio-sarcoma (malignant glioma)	Glioma sarcomatodes
Melano-sarcoma	Melanoma sarcomatodes or
Melanotic sarcoma	Chromatophoroma.

III. Tumors commonly included among the sarcomas, but belonging elsewhere.
    Endothelioma
      Perithelioma
      Cylindroma
    Mixed tumors of sarcomatous appearance and behavior.

The origin of the tumor is unknown. Indications point to a focal beginning, some cell or small group of cells through whose abnormal vegetative activity it is begun and maintained. There is no evidence of extensive or continuous transformation of normal into tumor tissue.

Opinions differ as to the nature of the tumor primordium. It is held by some of the best authorities that sarcoma arises, through anaplasia from the differentiated normal tissues. Adami champions this view in these words:

"It is perfectly conceivable that in a highly developed tissue, or in a typical blastoma, certain cells can lose their specific properties and revert to a simple stage; that as the regenerating muscle fibre reverts towards the sarcoblastic type, so the cells of rhabdomyoma, being unable to function, are therefore all the more liable to lose their functional differentiation and assume a vegetative sarcoblastic type. In this there is nothing improbable. According to the hereditary characters impressed upon them, according also to the surroundings in which they find themselves, so will the cells attain to a certain stage of differentiation. And so a tumor may show any stage, from the very lowest round cell vegetative type, up to the (not quite perfectly) differentiated tissue cell. Being under abnormal conditions, and unable to function normally, the tumor cell can never, and never does, acquire perfect differentiation."

Holding this view, Adami naturally sees the connective tissue cells running the whole gamut of anaplasia. He continues:

"These vegetative, or 'embryonic' types of cells are simple and their range is comparatively small, from the small round cell, to that with larger amount of cytoplasm and rounded nucleus, to the oval cell, likewise with relatively abundant cytoplasm and oval nucleus, and the spindle cell still larger, with oval or even spindle-shaped nucleus and relatively less cytoplasm; though here we note a difference: we may have a small spindle-celled or a large spindled type of cells. In this way we distinguish the several forms of sarcoma: (1) the small round celled, (2) the round celled, (3) the large round celled, (4) the oat-shaped celled, (5) the small spindle celled, and (6) the large spindle celled. We classify according to the preponderating type of cell. Where, as in one order of growth, we find considerable variation in type, we speak of (7) the mixed cell sarcoma."

But the cells of sarcoma usually bear but a superficial resemblance to those of adult tissue; they more closely resemble those of embryonal tissue. But they are not exactly like embryonal tissue; certainly they do not usually behave as such. If the cells were embryonal, they should manifest some evidence of a tendency to eventual differentiation. This they rarely do. From sarcoma cells little is to be expected but more sarcoma cells. In those cases in which the tumor, as in fibro-sarcoma, chondro-sarcoma, and osteo-sarcoma, shows some admixture of differentiated tissue elements, the tumor primordium may have been complex, each of its components proceeding to vegetate or to differentiate according to its inherited tendencies.

There seems to be no legitimate reason for supposing that sarcomas differ from other tumors in regard to their beginnings; if most tumors develop from a primordium consisting of embryonal substance, sarcomas may do the same. That sarcomas, above other known tumors, are prone to develop after injury, does not affect the case. Some stimulation must excite the growth of the primordium. Perhaps too much stress has been laid upon the matter. Gross placed the number of cases resulting from trauma at 50 per cent; Escher, 39 per cent. Coley's 970 cases of sarcoma with a history of traumatism in 225, or 23 per cent. Meyerding in his study of sarcoma of the long bones found a history of trauma in 52 per cent.

The proponents of the traumatic theory, for the most part, adhere to the idea of a normal adult tissue primordium, and suppose its injury to be followed by regenerative activities during which the anaplasia is initiated. It is conceivable, as Adami points out, that anaplasia of the connective tissues might carry the cells back to the most primitive form of round cell, and that their rapid multiplication might lead to round cell sarcoma. But if that were the

case, one would expect round cell sarcoma to be as frequent in one tissue as in another, whereas it nearly always originates where lymphoid tissue occurs, and seems to spring from it.

That a sarcoma consisting of small round cells should originate from lymphoid tissue is, however, in no manner opposed to its origin from a primordium of residual embryonic lymphoid cells, for the place, above all others, in which to expect such a primordium would be where lymphoid tissue was normally to be formed. The same would hold true of other varieties of the tumor; the occurrence of the spindle cell tumors in the fibrillar tissues would be expected as those tissues must have been derived from fibroblastic tissue, etc.

Sarcoma is commonly stated to be a tumor of early life. In making tumor diagnoses some look upon occurence before the 35th year as being in favor of sarcoma, and after it, as opposed to sarcoma, in cases in which the nature of a tumor is doubtful. In 109 cases of sarcoma of the long bones studied by Meyerding, the average age of the patients was 26.6 years.

Too much stress should not be placed upon the age at which the tumor occurs. From averages of great numbers of cases, the appearance of sarcoma is found to be ten years earlier than that of carcinoma, but sarcomas may occur at any age. This is well shown in the following tabulation taken from W. Roger Williams, "Natural History of Cancer," which shows the age of onset in 200 cases.

	Under 5 years	5	10	15	20	25	35	45	55	65	75 and upwards	Totals	Average	Maximum	Minimum
Males	2	2	6	6	7	22	10	20	16	8	1	100	40.4	79.0	2.0
Females	7	1	6	8	12	13	11	25	11	5	1	100	36.7	78.4	0.5

Wherever and however they arise, sarcomas usually form rounded nodular tumors whose rapid increase is usually the first thing to excite suspicion.

The rapidity of growth, however, is subject to great variation. In some cases the tumor grows slowly for years, and the first indication of malignancy is shown by recurrence after excision. This is exemplified by certain sarcomas of the skin, which grow more rapidly after each operation, and not until there have been a number of recurrences become metastatic. In other cases the growth is rapid, and metastasis early. A few sarcomas, therefore, may last for years, while others destroy life in the course of a few months.

The size to which the tumors develop frequently depends upon the rapidity with which metastasis occurs. Early metastasis may destroy the patient before the primary tumor is larger than an orange.

Peripherally situated tumors early reach the surface, distending the skin which is usually thinned and marked by large veins. As the substance of the

tumor is incapable of differentiation, traumatic injury, to which its position exposes it, is apt to be followed by ulcerations which do not heal. The tumor is then apt to fungate through the wound as a necrotic, hemorrhagic mass prone to infection.

The consistency of sarcomas varies. As they consist essentially of cells, they are nearly all soft, but admixture with more or less differentiated connective tissue, such as occurs in the complex varieties gives some of them an unexpected density and firmness. On the other hand, they are prone to degeneration and necrosis, so that they may be extremely soft, contain areas of softening, and even be cystic.

There is scarcely any tissue or organ of the body in which they do not occasionally occur. The most frequent seats of occurrence, however, are the subcutaneous, submucous, subserous, intermuscular, periosteal and lymphoid tissues.

The rapid growth of their cellular structure calls for abundant nourishment, and the formation of vessels more rapidly than their structure can be perfected, so that of all the tumors their blood-vessels are the most imperfect. In the most rapidly growing tumors many vessels consist of nothing but the endothelium, and in not a few cases the blood circulates between the cells of the tumor without any protection. This predisposes to early metastasis, and explains why it takes place by blood distribution.

Sarcomas grow by interstitial expansion, and by peripheral infiltration. It is unusual for them to be encapsulated. They may be circumscribed, and where the adjacent tissue is more easily pushed aside than invaded, partial encapsulation may occur. Veins are first pushed aside and flattened, then invaded, their cells penetrating the interior where masses occasionally extend for considerable distances, and may at any time break loose to become tumor emboli. This is a second reason why metastasis so regularly takes place by way of the blood. Metastasis by way of the lymphatics does, however, occasionally occur.

The complex varieties may be accounted for in two ways; either the tumor may develop from a complex primordium, or cells of the adjacent and invaded tissues surviving in the midst of the tumor cells may continue their normal function, and through multiplication and differentiation in the abnormal environment form fibrillar, adipose, chondrous, or osseous tissue respectively. But some of the cells of the tumor may be conceived to differentiate.

Tissue heterologous to that in which the tumor is growing is frequently attributed to metaplasia.

1. SMALL ROUND CELL SARCOMA

Lympho-sarcoma or lymphocytoma. This is a highly malignant tumor arising from the lymphoid tissues, composed of small round cells, characterized by rapid growth, infiltration of the neighboring structures, and early metastases through the blood.

There seems to be at present a strong and wise tendency to abandon the name small round sarcoma, and to substitute lympho-sarcoma.

Concerning the origin of the tumor, the following theories may be considered:

(*a*) The tumor originates from the connective tissues through the phenomenon of anaplasia.

(*b*) The tumor originates through abnormal vegetative activities of the lymphocytes in the lymph-nodes and other lymphoid deposits in the various

FIG. 207.—Section of the wall of the stomach in which a primary lympho-sarcoma has invaded the musculature; in one place it has extended through to the serosa. (*Broders.*)

tissues of the body. If from the lymph-nodes, through continuous multiplication of the lymphocytes until their architecture is destroyed, and the capsule being penetrated by the invading cells, widespread infiltration of the surrounding tissues occurs. If from other lymphoid deposits, not definitely collected in nodes, through continuous and infiltrative growth.

(*c*) The tumor originates from lymphoblasts, that is, from the undifferentiated cells of the germ centers of the lymph-nodes. If these cells multiply rapidly and without differentiation, there results a tumor composed of small polyhedral cells separated by a delicate fibrillar stroma and blood-vessels; if they differentiate, a tumor composed of lymphocytes.

(*d*) The tumor originates from embryonal residual cells.

The tumor forms a soft rounded mass, circumscribed, but not encapsulated, section of which has a uniform pinkish, or pinkish gray color. It may show numerous red dots that are usually cut vessels, or distributed red areas, which are interstitial hemorrhages.

They are rarely larger than a small orange, because the metastatic secondaries so early destroy life.

Upon microscopic examination either of two types of structure may be found:

1. The tumor is composed of fairly typical lymphocytes, many in active mitosis, separated by a very small, quantity of amorphus, usually invisible, intercellular substance—"kittsubstance." The numerous small vessels are composed of endothelium only.

2. The tumor is composed of a slightly larger type of cell, with more cytoplasm, larger nuclei and a polyhedral shape, separated by a fairly regular reticu-

lum of delicate connective tissue fibres. This type is commonly described as
lymph-adeno sarcoma.

When a single tumor of either of these structures occurs in the subcutaneous,
submucous, subserous, intermuscular, periosteal, meningeal, ovarian, testicular,
or other tissues, the diagnosis is usually easy. All that is necessary is to exclude
the possibility of its being a subacute inflammatory infiltration. But if it
arise definitely from the lymphatic tissue, it is necessary to exclude leukemia
and the aleukemic form of lymphatic leukemia before the diagnosis can be
completed.

This is one of the most malignant types of tumor, the duration of life from
the time of its first discovery rarely being longer than two years. It returns
promptly when excised, and gives metastasis through the blood vessels very
early. But it is highly susceptible to the destructive effects of X-rays and
radium, and some cases that the surgeon must have regarded as hopeless have
been cured.

2. Large Round Cell Sarcoma

Concerning this tumor Ewing says: "These tumors may, as a rule, be divided
among the endotheliomas, tumors of lymphoid cells, carcinomas, and sarcomas
of which the cells are not strictly round." It is quite probable that there is no
such definite entity as the large round cell sarcoma and it might be well to
abandon the name altogether. But it appears in nearly every book on path-
ology, and cases are constantly reported.

The tumors, called by this name, that have been brought to our notice
have usually proved very puzzling, but the appropriateness of the diagnosis was
doubtful. Some were fragments of sarcomas in a very decadent condition from
some kind of retrogressive change by which some of the cells were enormously
swollen, and contained immense nuclei, while others were of normal or about
normal size. Others were histologically of a structure not to be certainly ex-
cluded from the carcinomas. In practically all cases there was considerable
intercellular fibrillar tissue, with more or less alveolar appearance.

3. Spindle Cell Sarcoma

This is a malignant tumor composed of spindle cells of varying size and shape,
separated from one another by a varying quantity of amorphous or fibrillar
intercellular substance.

At first thought nothing ought to be more easy than to make the diagnosis of
a tumor composed of such strikingly characteristic elements as spindles; but
unfortunately the matter is not quite so simple as it seems.

The typical cell concerned is the fibroblast—or at least a cell that corresponds
with it in appearance—and a benign tumor composed of such is, according to
Mallory's nomenclature, a *fibroblastoma*, an excellent example of which is seen in
the "dural endothelioma." If the fibroblasts differentiate and form collagen,
fibroglia and elastica, *fibroma*, another benign tumor results, in which there may
be few or many spindle cells; if the cells do not differentiate and the tumor be

malignant it is "fibro-sarcoma" according to Mallory, or spindle cell sarcoma in ordinary parlance.

Tumors of unstriated muscle are also composed of spindle cells, and though, when typical, the cells can be differentiated from fibroblasts with ease, they sometimes resemble them closely.

Epithelium, especially of the basal layers of the skin, the pelvis of the kidney and the wall of the bladder, may have cells of spindle shape, and sometimes forms great masses of them.

Growing granulation tissue consists largely of fibroblasts, and not infrequently so closely resembles sarcoma as to make an experienced pathologist

FIG. 208.—Large spindle-cell (?) sarcoma of the right thigh. The large superficial veins that usually ramify upon the surfaces of such tumors show very distinctly. (*From a patient of Dr. Wm. L. Rodman's in the Medico-Chirurgical Hospital of Philadelphia.*)

hesitate about the diagnosis unless he knows the source and history of the material he is examining.

When the inflammatory connective tissue hyperplasias are ruled out through knowledge of the source of the material and the history of the case, the epithelial tumors through knowledge of their origin from the epithelial surface tissue of the locations mentioned, the muscular tumors through knowledge that they arose from the uterus or the alimentary canal and perhaps through demonstration of their myoglia fibrils, the dural endothelioma through knowledge of its source and history of slow development, and so on, there still remain a number of tumors composed almost exclusively of spindle cells, that are usually characterized by rapid growth and intense malignancy. They are the spindle cell sarcomas.

They are for the most part, definite, circumscribed tumors, and arise from the subcutaneous, submucous, subserous, irntemuscular, areolar and periosteal

connective tissues, the bone marrow, and sometimes from the framework of the organs, forming nodes of more or less regularly rounded form, commonly partly encapsulated. The growth is usually rapid, though sometimes slow at first, and rapid later. Excision of the growth is usually easy when it is small, but later becomes complicated by a distinct tendency to infiltration. The tumor almost always returns shortly after operation, and usually grows more rapidly than before. It is usually a single tumor, but may be multiple. It is painless, and patients are frequently deterred from seeking surgical advice because the swelling does not bother them.

If the tumor attains to a considerable size, large, distended veins ramify over its surface.

The tumor rarely moves easily, as it has numerous infiltrative connections with the surrounding structures. The firmness and mobility differ in different cases. Some of the tumors are hard, some quite soft. Tumors originating about the bones seem to attain the largest size, but they rarely reach a size greater than a cocoanut before metastasis ends the life of the patient.

External tumors becoming injured frequently ulcerate and fungate.

When a tumor is incised, the cut surface varies according to its purely or partially cellular structure. The purely cellular tumors are grayish pink in color, and uniform in texture, the more fibrillar ones fasciculated and paler. In many cases there are dots or splotches of red or red-brown color, indicating hemorrhage, and sometimes there are more or less gelatinous and cystic areas where mucoid degeneration or necrosis has occurred. Necrotic areas usually appear yellowish in color.

When examined histologically the tumor is found to consist essentially of spindle cells. But here there is considerable latitude of interpretation. In some cases nothing but cells can be found; in others the cells are separated by a small amount of fibrillar substance; in a few cases there are many well-formed fibres easily recognized as collagen.

The cells vary greatly in appearance. Some are very short and have rounded nuclei, as in Adami's oat-shaped celled sarcoma, others are short spindles with ovoid vesicular nuclei, still others are large, so as to be justly called large spindle cells. The cells are by no means always frankly of the spindle shape, but this is to be expected if one is familiar with the true appearance of the fibroblasts, which are not really spindle shaped at all but elongate, and branched at the ends. The spindle shape seems to be an optical effect resulting from the arrangement and approximation of the cells in parallel strands. When they are separated from one another, their natural irregularities and inequalities become evident. Opportunity for observing this is to be found in edematous tumors, in which the cells are frequently widely separated, and unfamiliarity with the normal appearance of the cells has caused some to suppose that there is another variety of sarcoma with irregular shaped cells—*irregular shaped cell sarcoma*, or *mixed cell sarcoma*.

The long diameters of the cells lying parallel, they appear to be collected in bundles that twist and twine about the blood vessels. The nuclei of the sarcoma spindles are vesicular. Rapidly growing tumors contain many cell

in mitosis, and bad preservation of the material and degenerative change, usually cause many of the karyokinetic figures to be deformed, and many of the nuclei to be excessively large or otherwise abnormal.

Fig. 209.—Malignant ossifying extraperiosteal sarcoma which produced pulmonary metastases. (*Ewing.*)

The tumors usually have numerous and imperfectly formed blood-vessels. Between the cells there may be nothing but an amorphus "Kittsubstanz," demonstrable only by specific methods of staining, or there may be fine fibres

of collagenous substance, or there may be considerable well-formed fibrillar intercellular substance. In general, the more purely cellular the tumor is, the more malignant it is; the more it contains intercellular fibrils the more slowly it grows, and the less malignant it is.

Care must be taken to know from what part of the tumor the fragment for microscopic examination is selected. At the edges of the tumor the invading
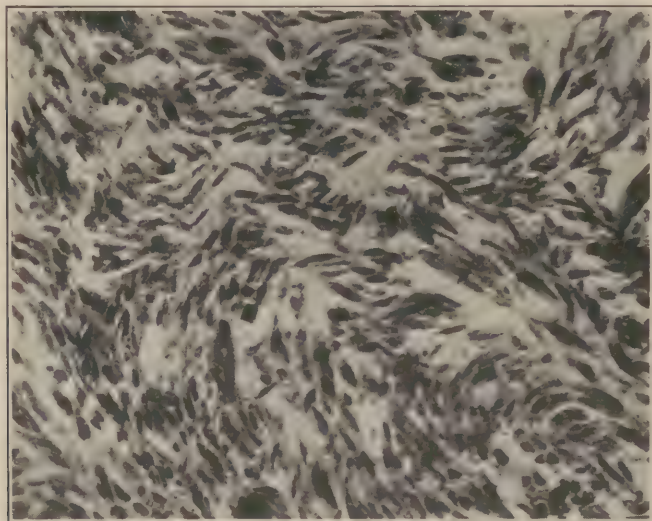
Fig. 210.—Microscopic section of a small spindle-cell sarcoma. (*Photomicrograph by Prof. Allen J. Smith.*)

cells insinuate themselves between the preexistent elements, and it is possible to mistake the antecedent fibrillar tissue for part of the tumor.

Spindle cell sarcoma of the skin and sub-cutaneous tissues may grow slowly, and although it returns again and again, the patient may live for years. On the other hand, spindle cell sarcomas arising from the periosteum may destroy life within six months.

Spindle cell sarcoma varies in its resistance to the destructive influence of X-rays and radium, which cannot be depended upon to effect a cure. Under these circumstances it would seem as through through surgical eradication should precede recourse to these agents.

4. Giant Cell Sarcoma

A giant cell sarcoma is one characterized by the presence of many giant cells. This definition is unscientific and results in confusion, but in the present state of knowledge there seems to be no way of clarifying it. In the first place, some, as Adami, doubt that the tumor is correctly classified as sarcoma, and view it as a form of bone marrow tumor—a myeloma. In the second place, it is frequently confused with conditions doubtfully classified as tumors. In reviewing the cases that have come under observation one find the following:

1. *Results of Cell Degeneration in Other Varieties of Sarcoma.*—Giant, and gigantic cells may be found in the unhealthy parts of many sarcomas.

They lie among decadent cells of all sizes and shapes, in which are many nuclear deformities and mitotic abnormalities, and whose cytoplasm seems inclined to coalesce. The giant cells themselves are as diversified in size and appearance as the cells among which they lie. Some are relatively small, yet have many nuclei crowded together, some are very large and have only a few enormous nuclei closely packed together. It is not the whole tumor, but only occasional parts in which such appearances are to be found, and it is evident that they should not play any part in its classification.

2. *Modified Granulation Tissue.*—This is best exemplified in the condition now frequently spoken of as Schlatter-Osgood's disease, which most frequently appears as an enlargement of the tubercle of the tibia after slight trauma or fracture of the beak-shaped process of that bone, and is characterized by painful enlargement lasting for months without considerable increase in size. It is rare, and Bloodgood observed only two cases. It is sometimes classed as a periosteal variety of sarcoma, but the X-rays show very little invasion of the osseous tissue, and when the part is curetted, or the affected tissue excised, cure may be expected. If the first operation is not successful, a second usually is, and the disease does not become invasive or metastatic, which is in marked contrast with the periosteal sarcoma, which almost always kills.

The histology of the lesion is peculiar. It is made up of a well vascularized tissue composed of miscellaneous cells, most of which are fibroblasts, but among which are a fair proportion of lymphocytes and plasma cells, and a considerable number of giant cells of varied appearance, some large, some small, some close together, others scattered. They do not have the peripherally arranged nuclei of the foreign body giant cells, or cells of Langhans, nor do they have the healthy vesicular nuclei of the myeloplaxes regularly distributed throughout their substance. They rather give the impression of morbid products resulting from cellular decadence.

3. *Tumors in Which the Giant Cells are Characteristic.*

A. Pseudosarcoma Gigantocellulare

These tumors now becoming known under the name "benign giant cell sarcoma" usually arise either from the bone marrow (central giant cell sarcoma) or from the periosteum, (periosteal giant cell sarcoma), though they may rarely occur in the soft tissues. They most frequently occur in young persons between 20 and 25 years of age about the long bones, especially from the lower end of the femur, the upper end of the tibia, the fibula, the humerus, the radius and more rarely on the alveolar process of the jaw (epulis) and the flat bones.

The appearance is sometimes preceded by mild traumatism, and is always painful, though the suffering is never acute. If they begin in the medulla: the shaft is slowly distended until it forms only a thin covering stretched over the tumor mass. If they begin at the cancellous tissue of an articulating extremity, they cause atrophy of the bony trabeculae, and gradually form a mass that extends to the surface, still covered by the superficial bony lamellae. In both cases the bone is so transformed that spontaneous fracture may occur.

When the tumor arises from the periosteum, the outer surface of the bone is slowly excavated, until the medullary cavity is reached.

If undisturbed giant cell sarcomas may attain to a great size; tumors as large as a human head are not infrequent. But as a rule, hemorrhagic extravasation and cell degeneration cause the cystic transformation of much of the tissue by that time, osteitis fibrosa with cysts follows, and the tumor spontaneously recovering. This giant cell tumor is not malignant. It is locally destructive, but not metastatic, does not recur when properly treated, and tends toward spontaneous recovery. Many authors now cease to include it among the sarcomas; Adami considers it a myeloma. Martland does not regard it as a tumor, but as an inflammation with exuberant granulation tissue. With this view Ewing is in sympathy, though not approving Barrie's designation "hemorrhagic osteomyelitis" which he thinks too suggestive of intense acute inflammation.

FIG. 211.—Foreign body giant cell tumor of the ulna. (*Meyerding*.)

The gross appearance varies according to the position in which it grows. When external it forms a large, rounded, well circumscribed, more or less nodular, highly vascular tumor, immovably attached to the bone from which it springs, and covered by periosteum, on which account it is said to be encapsulated. When centrally situated, it distends the shaft to a large spindle. A radiogram usually shows it to be cystic and covered with a layer of bone.

Section of such a tumor may be made without difficulty, though bony trabeculae may be scattered throughout its substance. The solid parts of the tumor are of a dark red or maroon color, and lack uniformity because of frequent hemorrhagic and degenerated areas. There are apt to be numerous cysts filled with chocolate-colored or serous fluid.

Histological examination in rare instances shows the matrix of the tumor to be composed of round cells, but spindle cells are the rule. Among them are some lymphocytes, occasional plasma cells, and the characteristic giant cells, usually distributed without much uniformity. They are definite and distinct, and not infrequently seem to lie in spaces which they nearly fill. They have glassy cytoplasm and many nuclei, that are distinct, vesicular and uniform. Occasional mitotic figures indicate that they multiply, and suggest that the giant cells are formed by multiplication of the nuclei without division of the cytoplasm. The cytoplasm is sometimes occupied by minute foreign bodies, and may be vacuolated. The surface of each cell is usually smooth, and no protoplasmic prolongations extend between the neighboring cells as in the giant cells of Langhans.

The histogenesis of the giant cells has been the subject of much speculation. As the tumors usually occur in the bones, it first occurs to everyone that there must be a connection between the two. Adami and others believe that they originate from the marrow; but many of the tumors are of periosteal origin, in which marrow can play no part, so that it may be that some of the giant cells are modified osteoblasts or osteoclasts. As the tumors are highly vascular at times, some see the giant cells arising through modification of groups of angioblastic cells, and view them as derivatives of the endothelium. As the giant cells commonly contain vacuoles, red blood corpuscles and spicules of bone, a few consider them to be foreign body cells. Finally, some have supposed the giant cells to be formed through the coalescence of neighboring degenerating cells.

The giant cell epulides sometimes differ from the other giant cell tumors in having a much more fibrillar matrix. Such are benign, and if removed, do not return. But occasional epulides with purely cellular matrices may be malignant tumors, return, grow into the antrum, and invade the bones.

The matrix of most of these tumors is a highly vascular fibroplastic granulation tissue. It appears to be chiefly composed of spindle cells, suggesting that the tumor is only a modification of spindle cell sarcoma. But this latter is a highly malignant metastatic tumor. The giant cell tumor does not behave like spindle cell sarcoma. It does not return when excised, and only in rare cases does it cause metastasis. The matrix of some of these tumors contains large numbers of large cells containing molecular fat (xanthoma cells). Such tumors are usually firm and of a yellowish color.

It is no longer thought necessary either to amputate the limb or to remove the entire diseased bone affected with this tumor. It is found to be sufficient to thoroughly remove the diseased tissue with knife and curet, and then submit the seat of operation to the X-rays. Some cases are successfully treated with X-ray and radium without operation.

B. Xanthic Tumors

Along the tendon sheaths, and more rarely in the fascias, small tumors, usually less than 3 cm. in diameter, occasionally make their appearance after injury or infection. The yellowish color of their cut surface has led to the designation xanthic, and uncertainty as to their precise nature makes it wise to employ that term until more definite information is available.

Less than a hundred cases seem to have been reported, and the best studies of them have been made by Tourneux, who in 1913, in a study of "Sarcoma of the Tendon Sheaths," collected some 93 cases, of which 54 probably fall into the class of new growths under consideration, and by Broders who studied 17 cases that were observed in the Mayo Clinic.

The growths are encapsulated, grayish, brownish or pinkish-yellow, lobulated tumors, whose substance is divided by strands of connective tissue derived from the capsule, and in the cut substance appear white. The consistency is firm and tough.

The histological structure is peculiar and has been so variously interpreted that the tumors appear in the literature under many names, among which are sarcoma, spindle cell sarcoma, myeloid sarcoma, myeloid tumor, myeloma, myeloid endothelioma, myeloxanthoma, granuloma, giant cell tumor and giant-cell sarcoma.

The explanation of this uncertain nomenclature is the varying basic cellular structure, and the presence in it of a variable but considerable number of giant cells.

As Broders concludes, it is highly probable that these growths are not tumors at all, but granulation tissue formations following injury with hemorrhagic

FIG. 212.—Typical giant-cell tumor containing numerous foreign body giant-cells.   ×100.
(*Meyerding*.)

extravasation of the tissue.   The basic structure is granulation tissue, and the giant cells are foreign-body giant cells engaged in assisting the removal of the debris.   But the unusual and characteristic feature is the presence of large numbers of foamy lipoid-containing xanthoma cells, situated, for the most part, at the periphery of the formation.   These probably are large lymphocytes or endothelial leucocytes or cells that have loaded themselves with the trans-formation products of the injured tissue and its exudates.   Broders found the vacuoles to give the lipoid reaction with Scarlet R, to give a positive reaction for iron, and in on case there were cholesterin crystals.   The color of the growths and the presence of the frothy vacuolated cells remind one of *xanthoma tuberosum*, and of the smaller lesions of *xanthelasma*, but the presence of giant cells sharply differentiates them.

One is also reminded that xanthic cells, with the typical frothy appearance, are frequently to be found in the benign giant-cell sarcomas of bone, and in the lesions of osteitis fibrosa cystica.

C. Sarcoma Gigantocellulare

Malignant giant cell sarcoma: Osteoclast sarcoma. This really malignant tumor is more rare and less well characterized. It is a kind of menace, for it complicates deductions made concerning the curability and benignity of the other forms, from which it may not be differentiated until repeated return and metastasis show its true nature.

It is, however, usually of a more uniform structure, and paler color. It lacks the cystic tendency, is less hemorrhagic, and its matrix consists of a less well-vascularized aggregation of spindle cells of much greater uniformity, among which the miscellaneous cells characteristic of developing granulation tissue are absent. The giant cells are more uniformly distributed. They are probably myelogenic or osteoclastic, and not foreign-body giant cells.

In the recurrent and secondary tumors the giant cells may be present or absent. They seem to have nothing to do with the behavior of the tumor, which is like that of spindle cell sarcomas without giant cells.

If the facts given in the paragraphs upon pseudosarcoma gigantocellulare be correct, more careful observation will be needed before this tumor, of whose existence there can be no doubt, can be differentiated from it.

Complex Sarcomas

These can be dismissed with brief mention. They consist of easily recognized, fairly well differentiated, tissues—adipose, fibrillar, chondrous, osseous, myxoid, muscular, etc.—in which, and confusing the structure of which, appear an excessive number of undifferentiated cells. It is on account of this excessively cellular quality supposed to be responsible for a different clinical behavior and malignant tendency, that name of the tumor is changed from fibroma, lipoma, chondroma, osteoma, myxoma, etc., to fibroma sarcomatodes, lipoma sarcomatodes, chondroma sarcomatodes, osteoma sarcomatodes, myxoma sarcomatodes, etc., respectively, from the histological point of view.

It is usually assumed that such tumors have their beginning in benign hyperplasia of a previously well behaved and normal tissue. But as usual, the primordium of the tumor is unknown. Whatever the origin of the cells, it seems clear that the varying benignancy and malignancy of the tumors may be referred to the tendency of the cells to multiply slowly and differentiate completely, in the first case, and to multiply more rapidly than they can differentiate.

In favor of the descent of these tumors from an embryonal and complex primordium seems to be the occurence of *myxo-sarcoma* or *myxoma sarcomatodes*, which scarcely can develop from preexisting normal tissue because no mucous tissue is normally to be found in the fully developed body.

The term should be restricted to those highly malignant tumors composed of myxoblasts, and characterized by immediate and continuous formation of connective tissue mucus.

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The presence of mucous tissue seems to indicate a malignant tendency on the part of many tumors. Bloodgood found that mucous tissue in sarcomas of bone was an almost sure sign of their eventual malignant tendency.

Angio-sarcoma requires additional mention as there is some uncertainty as to what the term implies. The difficulty has been mentioned in the sections upon angioma and upon endothelioma which the reader should peruse. To

FIG. 213.—Roentgenogram of a chondro-sarcoma of the left femur. (*Meyerding.*)

many, angio-sarcoma is but a variety of angioma; to others it is a variety of endothelioma; to still others, it is a special variety of endothelioma in which the cells bear a definite relation to the blood vessels, which they surround—perithelioma. Careless students sometimes apply the term to tumors whose only title to it lies in the fact that they are unusually vascular.

It would be well to restrict the term to malignant tumors characterized by initial and continuous new formation of blood-vessels associated with an excessive number of cells resembling those of sarcoma.

The cells engaging in the formation of the vessels are certainly angioblasts and either endothelial or very nearly related to them. With those, therefore, who hold that these tumors are endotheliomas there can be no serious difference of opinion, until it comes to the nature of the intervascular cells, which do not look like endothelium, or behave like it, and may bespeak complexity of the primordium from which the tumor has its beginning.

The perithelial form of angio-sarcoma is characterized by the occurrence of cells so definitely arranged about the blood-vessels as to appear to have some definite connection with them and possible origin from them. Some suppose them to be derived from the endothelium lining the vessels, others from the endothelium of the perivascular spaces. But the great mass of the cells of the

body of the tumor, when they are not destroyed by necrosis, are spherical and totally unlike the vascular endothelium, and it is highly improbable that such imperfectly formed blood-vessels as occur in sarcoma ever have perivascular lymph spaces. That a few fibres from the vessel wall occasionally separate the cells in close juxtaposition to it means little. Upon newly forming vessels

Fig. 214.—Perithelioma. A sarcoma whose cells seem to surround blood-vessels in a definite manner. (*Photomicrograph by Prof. Allen J. Smith.*)

fibroblasts extend to furnish it with its adventitia, and the fibroblasts by which these are formed are well known to insinuate themselves between adjacent cells where their fibres may be formed abnormally and among which they may be scattered.

Vascular sarcomas and angio-sarcomas sometimes show a curious hyaline or mucinoid transformation of the vessel wall, or of the cells in its immediate neighborhood, so that considerable lengths of the vessels may be surrounded by structureless tubular encasements. This appearance characterizes the *cylindroma* which is not a special or definite variety of tumor.

Chromatophoroma: Melanoma: Melanotic Sarcoma

In a position so intimately connected with sarcoma on the one hand, and carcinoma on the other hand, that it is impossible properly to classify them are certain cellular tumors variously known as *melanotic sarcoma, melanosarcoma, melanoblastoma, melano-carcinoma, melanoma,* and *chromatophoroma.*

These highly malignant tumors are most commonly known to the surgeon as melanotic sarcomas. But this time-honored designation is doubtfully correct.

The difficulty of classification is very old, and was fully appreciated by Virchow, who first suggested that the tumors be called *melanoma* as not committing to any definite origin.   Ribbert has suggested the name *chromatophroroma* as defining its most probable origin.

The most common seats of occurrence are the skin and the eye; rare tumors of the same (?) kind occur in the esophagus, the rectum, the liver, the common bile ducts, the gall bladder, the pars prostatica urethra, the adrenal, the ovary, the spleen and the meninges.

FIG. 215.   FIG. 216.

FIG. 215.—Melanotic sarcoma of the eye. (*From a specimen in the Museum of the Philadelphia General Hospital.*)
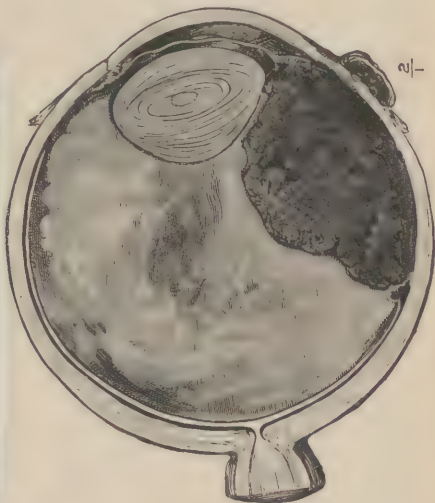
FIG. 216.—Lateral half of an eye-ball containing a melanotic sarcoma of the ciliary body. There is a small extraocular nodule over the seat of one of the anterior perforating vessels, a short distance from the sclero-corneal margin. (*Specimen in the Royal London Ophthalmic Hospital Museum.*)

The study of pigment production among animals generally gives the impression that it is a function of certain mesoblastic cells known as chromatophores. Such cells exist in many parts of the human body.   In the skin a number can always be found in the papilla of the corium and insinuating themselves between the lower layers of the epidermis to which they are supposed to convey pigment prepared in their own substance, distributing and collecting it so that under normal conditions it is only to be found in the pigment layer.   Chromatophores also occur in other parts of the body, either in considerable masses as in the iris, ciliary body, choroid, and pigmented layer of the retina of the eye, choroid plexus of the brain or distributed throughout the tissues generally so sparsely as rarely to be found.   These chromatophores vary considerably in appearance, but for the most part are rather large cells of more or less pronounced spindle shape, with considerable cytoplasm.   They may be polyhedral and epithelioid. The characteristic feature is the presence of granules of iron-free metabolic pigment—melanin—in the cytoplasm, presumably formed through their metabolic activities.   This pigment varies in color from yellow brown to almost black.

It gives the varying shades of color to the skins of the different races, the different colors to the eyes of different individuals, and makes the ciliary body, choroid, and pigmented layer of the retina black. It is also the pigment of the hair.

It is from these chromatophores that Ribbert believes the tumors to be derived. But it is the differences in the size and shape of the cells found in the tumors that are difficult for the pathologist to understand. Many of the
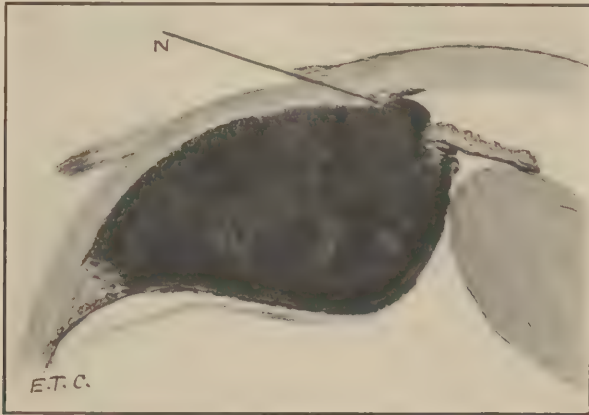
FIG. 217.—Melanotic sarcoma of the ciliary body, extending forward through the root of the iris, and appearing in the anterior chamber at *N*; also infiltrating the spaces of Fontana. (*Collins and Mayer.*)

tumors originating in the skin are composed of cells of such large size and distinctly epithelial appearance, as to incline him to regard them as carcinomas; while most of those that arise in the eye are composed of smaller cells of spindle shape that he would be inclined to consider as sarcomas. In each case the diagnosis corresponds with the clinical behavior of the tumor. Are there, then, both melanotic carcinomas and sarcomas?

The pigmented tumors of the skin most commonly arise from antecedent small congenital defects related to the tumors, and known as cellular naevi. If the nature of the cells of which the naevi are composed could be determined, it might aid in determining the nature and origin of those of the larger, more important tumor, and malignant chromatophoroma.

Cellular Naevi.—These are commonly known both to the profession and laity as "moles" or "pigmented moles," or when scarcely pigmented, as "soft moles." They are extremely common, and almost everybody has one or more upon his skin. They are congenital and commonly appear at, or shortly after, birth, as soft slightly elevated brownish spots with a velvety surface. The appearance, however, varies, and Unna has described four which he conceives to correspond to stages of growth and development. They are:

1. Flat embedded naevi.
2. Nodular elevated naevi.
3. Berry-like divided naevi.
4. Soft molluscum.

The size of the lesions varies; as a rule they are inconsiderable and inoffensive, but they may cover square feet of surface and be unsightly and injurious. Occasionally they occur with a peculiar symmetry, as in the so-called "bathing-trunk type" which affects the skin of the lower part of the abdomen and of the upper parts of both thighs.

The velvety appearance of the surface is partly due to the presence of delicate lanugo hairs. Large and coarse hairs may also be present singly or in considerable numbers.

FIG. 218.

FIG. 219.

FIG. 218.—A dark-colored fungus-shaped pigmented naevus from the buttock of a young man of 22 years. Its surface was divided like a raspberry, and sparsely covered with long coarse hairs. (²⁄₃ actual size.)

FIG. 219.—Little girl with large hirsute pigmented naevi. (*Patient of Dr. Bradley's in the Philadelphia General Hospital.*)

The first microscopic studies of these defects seems to have been made by Demieville who found them to be composed of columns and alveoli of cells ascending toward the epidermis, and descending into the cutis. The cells in these nests are usually small, cuboidal or elongate, and show large oval vesicular nuclei. In each there is usually a varying quantity of pigment. Between the cell columns connective tissue fibres are present in varying amounts, but between the cells themselves, there is neither collagen nor elastica. The origin of the cells is the matter in dispute. von Recklinghausen taught that they arose from the endothelium; Orth, following Unna, that they were epithelial. Hartzell following the latter school supposes that some of the cells of the basal layer of the skin are accidentally snared off during embryonal development, and are thereafter sequestered in the derm where they multiply slowly during many subsequent years. From this point of view they belong in the class of congenital defects known as enclavomas. But, a critical examination of naevi shows that their cells do not resemble those of the basal layer of the epiderm, but are smaller less regular in shape, frequently spindle or stellate, and that a delicate reticulum does penetrate between them. On this account Ribbert believes that they have nothing to do with the epiderm or with the epithelium, but are chromatophores, congenitally and defectively accumulated in mass formation. As the

chromatophores are conceded to be of mesoblastic derivation, any accumulation of them or tumor derived from them must be the same, so that from his point of view the chromatophoroma is not incorrectly designated sarcoma. It is only a special variety of sarcoma—melanotic sarcoma.

This view is also supported by the occasional occurrence of these tumors in parts of the body in which no epithelium is present, and by the definitely spindle shape of the cells of many of the tumors, especially those that occur in the eye.
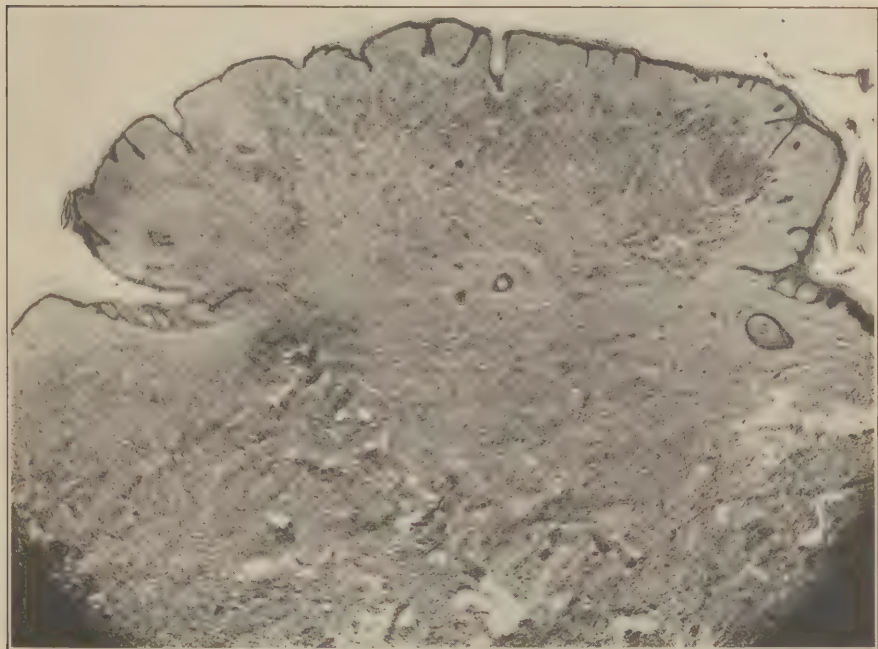
FIG. 220.—Slightly magnified section through an entire small pigmented naevus, showing its thin but regular epithelial covering, and the perpendicular columns of naevus cells below. (*Dr. F. D. Weidman.*)

It is also supported by the behavior of the tumor which usually gives early metastasis through the blood-vessels and only rarely, and apparently only when growing in the skin, through the lymphatics.

Opposed to Ribbert's view is the epithelial-like appearance of the cells of many of the dermal tumors and their tendency to metastasize through the lymphatics.

Can it be possible that there are two different pigmented tumors of different derivation, one arising from the epithelium, the other from the connective tissues? But if so, how account for the presence of the pigment in the former? Or can it be possible that in the dermal tumors there is simultaneous growth of both the chromatophores and epithelial cells the former furnishing the pigment to the latter?

We have examined certain skin tumors in which were groups of large cells of distinctly epithelial appearance, and suggesting nothing so much as cancer,

separated by strands and columns of highly cellular tissue largely composed of small spindle cells so deeply pigmented as to be visible to the naked eye as black stripes.   In such cases it seems difficult to imagine that two such differing types of cells can have the same origin.

FIG. 221.—Microscopic section of a pigmented naevus, showing the normal squamous epithelium of the skin except on the left where the clusters and columns of naevus cells are distinct.   (*Photomicrograph by Dr. F. D. Weidman.*)

But the whole behavior of the chromatophoroma is peculiar and irregular. Some of the primary tumors contain scarcely any pigment, others are almost jet black throughout; still others streaked or spotted with dark pigment. From a scarcely pigmented primary tumor, black secondaries may arise, or from a black primary tumor, almost colorless secondaries arise, or from either variety, some of the secondaries may be streaked or spotted with black.

The pigmented tumors usually grow very rapidly, forming nodes, the more superficial of which usually show the characteristic dark color.

If removed, they usually quickly return, and do so again and again.   Metastasis usually comes early, so that very large tumors are exceptional.   But whether metastasis comes early or late and takes place by the blood-vessels or the lymph-vessels differs greatly according to the origin and seat of occurrence of the tumor.

1. *Pigmented Tumors of the Eye.*—These may develop from the pigment cells of the choroid, from those of the ciliary body, or very rarely from collections of pigment cells that sometimes occur in the conjunctiva near the limbus. The tumors of the choroid may occur in nodular form, projecting into the cavity of the vitreous, or may extend between the sclera and retina as flattened dissecting discs. Those on the exterior of the globe are nodular. The latter can be observed with the naked eye, the former only with the ophthalmoscope. Either of the intra-ocular tumors sooner or later fills the eye, penetrates the tunics, and then fungates externally. Metastatic distribution of the tumor cells takes place under conditions that are very peculiar and interesting. For example, in some cases the tumor is detected when very small, and the globe of the eye at once removed. There may then be no recurrence of the tumor in loco, and the patient may think himself safe from danger. But sometimes in five years, sometimes in ten years, and occasionally as long as twenty-five years after, he suffers from multiple pigmented tumors of the viscera, especially the liver. How early the cells of the tumor begin to distribute themselves cannot be known, as there is no way of recognizing them unless they develop into secondary tumors. It would seem as though great numbers of cells must disseminate throughout the circulatory stream, reaching many parts of the body, in only a few of which successful colonization was possible, and then only after a long interval during which the cells were becoming accustomed to the new environment, or awaited satisfactory chemical conditions for growth.

Melanotic sarcomas of the eye usually extend to the optic nerve quite early, causing retro-bulbar nodular formations. So it comes about that whether the globe of the eye be removed or not, the orbital cavity may eventually become filled with the tumor, which later projects as a fungating, black, ulcerated, mass. This can, however usually be prevented by sufficiently early enucleation of the globe.

The cells composing these tumors are usually of the spindle shape, and their appearance and clinical behavior suggest only sarcoma.

2. *Pigmented Tumors of the Skin.*—These usually arise from "moles" or pigmented naevi, especially after injury. Enlargement and darkening of the mole is said to be the first indication of the impending tumor formation. It seems wise to recommend that when a mole is observed to darken or enlarge, it be removed; but that when it is inactive, it remain untouched. Efforts to remove moles by the use of caustics and similar agents have sometimes resulted in their unexpected growth. If it be decided to remove a mole, it should be done with the least possible disturbance of the mole itself, and with a wide margin of the surrounding normal skin, lest the disturbance arouse some of its outlying cell groups to activity.

Once tumor growth of the mole begins, it is difficult to predict what will happen; the behavior is just as irreglar as in the pigmented tumors of the eye. In some cases a considerable tumor mass of dark color forms at the seat of primary trouble, and may attain to the size of a walnut or a hen's egg before signs of metastasis appear; in other cases without much visible change in the mole, enlargement of the regional lymph-nodes makes its appearance. In the former

case, benefit may be expected from excision, but, in the latter, little can be hoped for. The tumor rarely proves to be amenable to the destructive effect of the X-rays or radium.

When sections of the primary tumor are microscopically examined, they usually show collections of cells of large size and epithelial appearance, more or less filled with pigment granules, which invade the corium and sub-cutis with
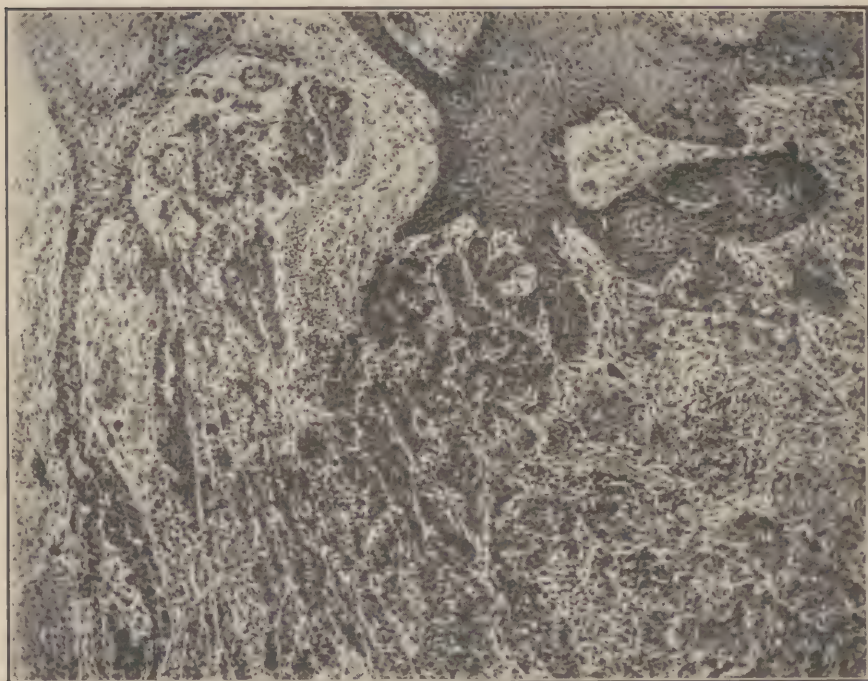
FIG. 222.—Microscopic section of a chromatophoroma growing from a "mole" on the skin of the breast. (×100.)

the formation of branching and ramifying prolongations similar to those characterizing squamous cell carcinoma, and partly surrounded and separated from one another by intervening fibrillar connective tissue. This carcinoma-like appearance with the added metastasis to the regional lymph-nodes impresses one with the carcinomatous nature of the disease. Gilchrist regarded such tumors as *pigmented carcinomas*, or *melano-carcinomas*. But not all of the tumors adopt this appearance; some are composed of masses of spindle cells of varying size with larger or smaller pigment contents, do not collect in alveolar formation like carcinoma, and frankly resemble sarcoma, differing, however, in their tendency to metastasize through the lymphatics instead of the blood-vessels. Whichever appearance is first adopted, the tumor cells eventually become admitted to the blood circulation, and the metastases may have a wide distribution throughout the internal organs.

In some cases the skin about the primary lesion becomes pigmented although not definitely infiltrated by the tumor cells. As the cells are added in increasing

numbers to the blood stream, diffuse pigmentation of the surface of the body occurs—melanoderma—and the pigment or its antecedents may be eliminated
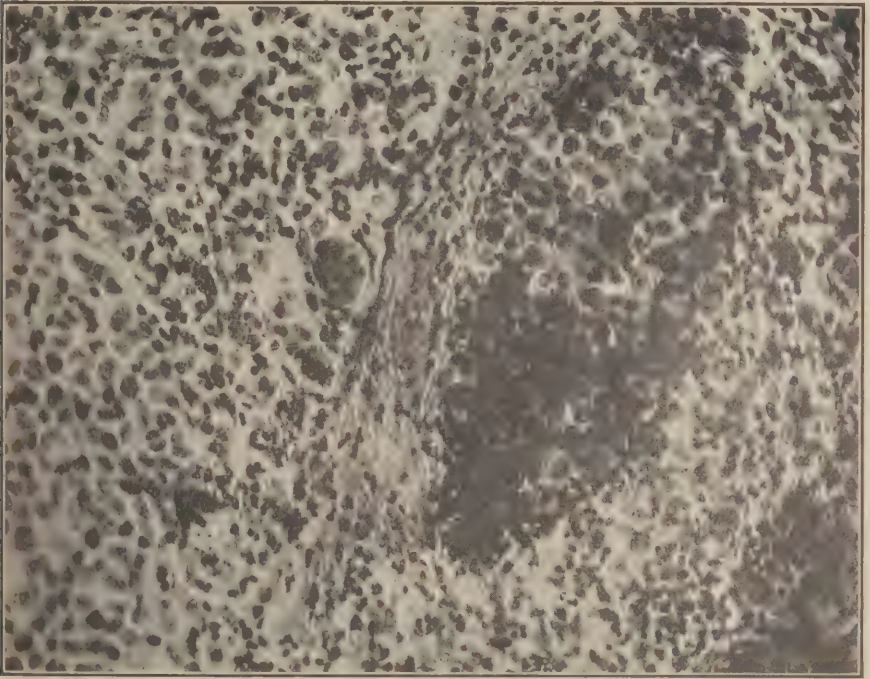
Fig. 223.—Microscopic section of the same chromatophoroma.   (×400.)
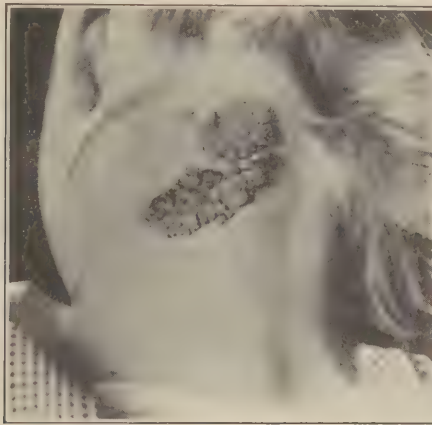
Fig. 224.—Naevus verrucosis on the back of the neck.   (*Dr. F. D. Weidman.*)

through the kidneys conferring upon the urine a dark color—melanuria—some-times evident as soon as the urine is passed, sometimes only after it has stood for a while.

The tumors of the skin are usually more rapidly fatal than those of the eye, and the patient rarely lives longer than eighteen months from the time of first discovery.

Most of the patients affected with these tumors are in the third decade of life.

3. *Internal Pigmented Tumors.*—These are supposed to arise from disseminated chromatophores and have a wide distribution, though they are of very rare occurrence. They sometimes make their appearance in the meninges, where they originate from the chromatophores of the pia, and either form nodes, or blacken the membrane by distributing great numbers of pigmented cells through its tissue. In that respect they behave much like secondary melanotic tumors of the meninges. Occasionally large pigmented tumors are found in the internal organs of individuals whose bodies fail to show any primary tumor from which they could originate through metastasis. Ewing has observed a large black tumor of the spleen in a case without any other discoverable tumor.

EPITHELIAL TUMORS

The tumors of this class are not composed of epithelium alone, but of epithelium and fibrillar connective tissue, the latter forming a fibro-vascular framework, upon which or in which the cells are regularly or irregularly disposed.

One of the most fundamental differences between these and other tumors, pointed out by Adami, is in the manner in which the cells are nourished. He says of the lepidic tumors—those of the epithelial group—"the blood-vessels do not penetrate the groups of specific cells in which there is an absence of definite stroma between the individual cells, although such stroma, of mesenchymatous origin, may be present between the groups of cells," and of the hylic tumors—the connective tissue group—"the specific cells lie in, and are separated by, a definite stroma, homogeneous or fibrillar, in which there may be or may not be blood-vessels and lymph-vessels."

Epithelial cells produce no intercellular products, either homogeneous or fibrillar, but are in immediate contact with one another, definitely arranged with reference to one another in tumors following the normal type of structure, and indefinitely arranged, in clusters or masses, in those departing from it.

Some of the epithelial tumors are difficult to bring into harmony with the fundamental conception of tumor as we have expressed it, probably because some of them are not tumors, but hypertrophies or infectious diseases considered to be tumors in the present state of ignorance.

For example: superficial epithelial tumors, if they maintain the typical arrangement of cells to matrix, are mostly described as papillomas; deep tumors doing the same as adenomas. But when these are individually and carefully examined, the former impress one as probable hypertrophies of epithelial covered papillary processes, and the latter as hypertrophies of glandular lobules. If they are hypertrophies, they cannot be true tumors. Upon further investigation, it is found that some of the papillomas, are definitely infectious diseases, depending upon demonstrable agents, running a more or less definite course, and

then tending to decline and eventually disappear.   Manifestly these are not
true tumors.

On the other hand, in those tumors of the group in which the cells abandon
their normal relationships, there is a tendency to infiltrate widely, so that there
results a growth lacking the circumscription by which tumor is ordinarily differ-
entiated from hyperplasia.   But at present it is customary to include these
differing lesions among the tumors, and attention is called to the inconsistencies
solely for the purpose of emphasizing the confusion that is inevitable from the
multiplicity and diversity of the pathological lesions collectively called tumors.

We find it convenient to divide the epithelial tumors into those respectively
characterized by the presence of squamous, columnar and glandular cells.

Squamous epithelium is nearly always stratified and transitional.   The lowest
layer—the basal cells—rest upon a basement membrane, each cell being in
contact with it and with neighboring cells on all sides, so as to present a cuboidal,
and sometimes even a columnar shape.   Suprajacent cells usually tend to spread
laterally, assuming a more and more flattened shape as they are forced upward
toward the surface by the multiplying cells below.   On the skin, the cells receive
an addition of eleidin or keratohyalin by which their substance acquires a
horny quality eventually forming the stratum corneum whose scale-like cells
finally desquamate.

These multiplying and transforming cells have no other source of nourish-
ment than the intercellular lymph derived from the cutis below and passed from
cell to cell, and it may be on account of advantage in its distribution that the
cells of the intermediate layers are provided with fine filamentous cytoplasmic
bridges between which are minute spaces.   The cells thus characterized are
known as *acanthus cells*, from the Greek, ακανθα, a thorn, but are perhaps more
frequently spoken of as *prickle cells*.   Tumors into which they enter as
conspicuous elements are sometimes called *acanthomas*, but as this term applies
equally to benign and malignant tumors, it seems to be of little practical use.

The horny change of the superficial cells is rarely seen except in the epiderm,
and seems to be a characteristic of surfaces subject to drying and friction.
Although other transitional squamous epithelia may be quite thick, no keratin
is normally formed.   Under pathological conditions, however, it may be found
where least expected, so that it may be a latent function of squamous
cells generally.

The squamous transitional epithelium of the pelvis of the kidney, the ureter
and the bladder is peculiar in the suddenness with which its superficial layers
become flat.   There is usually a basal layer of cuboidal shape, surmounted by
many layers of columnar or spindle shape, then a flattened layer.   This occa-
sional spindle shape of the squamous epithelial cells should be kept in kind, as
great aggregations of such spindle cells are sometimes found, and may lead to
the erroneous belief that the cells are of connective tissue origin.

Columnar or cylindrical epithelium occurs in the respiratory tract as a strati-
fied and transitional tissue, but everywhere else as a single layer of cells of
distinctly columnar shape, regularly arranged upon a basement membrane.
A definite polarity is maintained, the nuclei usually being in the lower third, and

the surface variously provided with an induration or condensation of substance, sometimes marked by striae—rodded epithelium—or provided with brush-like cilia—ciliated epithelium.

Seen from the upper surface, the appearance is much like that of a mosaic pavement. Such a delicate structure affords little protection against external agents, so occurs only upon unexposed surfaces.

The cells not only act as coverings, but also furnish lubrication through the secretion of mucin, which, accumulating in the distal two-thirds before leaving the cells, distends them in a characteristic manner, "goblet cells." This secretory function enables invaginated portions of the surface covering to act in lieu of glands—mucus glands. Other specialized columnar cells, as those of the glands of Lieberkühn of the intestine, are secretory.

The glandular epithelium varies. In the tubular glands of the stomach, intestine and uterus, this is of the cylindrical or columnar form, and in the ducts of most glands is of that shape. But in the largest and most important glands, the liver, kidneys, pancreas, mamma, etc., it is cuboidal, though differing in shape in the different glands, and in different parts of the glands.

These different types of epithelium appear in different tumors, which are usually easy to classify accordingly. But anaplasia sooner or later modifies the cells, causing them to revert to an indifferent or unspecialized more spherical shape, thus masking their original type. Anaplasia is supposed by many to lead into metaplasia. It is, of course, to be understood that the epithelial cells, no matter how complete their anaplasia, never transgress the blastodermic limitations—never, for example, become transformed into connective tissue of any kind, or into muscle, or vessels. The metaplastic modifications are limited to change from one type of epithelial cell to another, and usually from the higher, the columnar, to the lower, the squamous. Squamous epithelia not normally productive of keratin may, however, form it under conditions that obtain in tumor growth.

In those epithelial tumors whose structure conforms in a general way to the normal arrangement, the cells may continue to derive their nourishment through the basement membrane from the lymph below, and usually remain in good health. In those tumors in which the normal arrangement is lost, and the cells grow lawlessly and accumulate in masses, no means is provided for furnishing them with food. Only those at the periphery of the mass are near enough to the source of supply to maintain active vegetation, those farther away soon cease to multiply, and as new cells are added at the periphery, the central cells die. This is sometimes described as the "cell masses outgrowing their nutrition."

In the tumors of the former class, the cells usually show little vegetative activity, and mitotic figures are few, and normal; in those of the latter class, the cells multiply rapidly and irregularly, and are frequently overtaken by malnutrition in the reproductive act. Parts of such tumors may show great numbers of mitotic figures, many of which are abnormal. General decadence of the cells is shown by excessive size of some—physalides—excessive number of nuclei in some, gigantic nuclei, lobulated nuclei, and vacuolation both of cytoplasm and nuclei.

Vacuolation of the cells of the atypical epithelial tumors is frequent, even among cells seemingly in good health. Such vacuoles seem to contain fluid in which protein in solution is sometimes precipitated by the fixing reagents, later appearing in stained sections as spaces in the cytoplasm, each of which contains a larger or smaller homogeneous dot of eosin, or other anilin dye staining substance. Such condensations have repeatedly been mistaken for parasites. But even more suggestive of protozoa are some of the vacuoles in which the central dot connects with the walls of the vacuole by delicate filaments which give the whole a rosette-like aspect.

The "Plimmer's bodies" of carcinoma cells, are probably artefacts having some such explanation. In some cases cancer cells appear to be inside one another, and as frequently they seem to contain lymphocytes, leukocytes, or red blood corpuscles. Some suppose this to be an indication of their phagocytic action, but it is not certain that these are actual inclusions; they may be misinterpretations depending upon the superposition of irregular and compressed cells. With respect to the leukocytes and lymphocytes the case may be different for they may erode their way into the cancer cells through enzymic action.

Malnutrition leads to areas of degeneration and necrosis, widespread throughout the tumor, some of which may conform to recognized types—fatty, mucoid, or hyaline.

The *stroma* of the epithelial tumors must also be considered.

In the regular, typical, and benign tumors it corresponds fairly well with that of the structure represented by the tumor. It grows as an essential part of the tumor, more or less regularly keeping pace with its cells. It is not like the capsule of the more simple tumors, composed of the fibrillar connective tissue displaced and accumulated by compression; it is newly formed, and will appear in the secondary tumors, if there be any.

In the warts and papillomas the growth of the epithelial and connective tissue go so regularly, hand in hand, that one wonders whether the epithelium covering the surface grows because the papillae have hypertrophied, or the papillae hypertrophied because the epithelial covering has increased.

In carcinoma there seem to be two sources of stroma: first, the antecedent connective tissue of the part affected, and second, its increase as the result of the stimulating effect of the tumor. Carcinoma stroma can perhaps best be studied in the metastatic growths in the lymph-nodes. Those structures have scarcely any connective tissue apart from their capsules, but so soon as metastatic carcinoma begins to develop, stroma appears in quantity, usually more or less in correspondence with what was to be found in the primary tumor. The newly formed tissue is typical and contains collagen, fibroglia, and elastica, in varying proportions. As the new formation of the connective tissue only occurs where it is in close approximation with the cancer cells it seems to be a reaction—hyperplasia—resulting from their presence.

But it is not a uniform reaction, and as will later be seen, cancers differ greatly in the quantity of connective tissue they contain.

The reaction is not due to the irritative effects of the degeneration of decadent cancer cells; it is most marked in those cases in which the cells seem least

disturbed—scirrhus—and least so where the cell degeneration is apt to be most pronounced—medullary. Moreover, the reaction varies among the benign tumors in the same manner. Some papillomas have scarcely any stroma, as the villous papilloma of the bladder, while others have much, as the coarser papillomas of the skin.

For reasons that will be abundantly shown later, inflammation is very common in the malignant epithelial tumors, but the formation of the cancer stroma must not be attributed to it.

In rare cases the cells forming the stroma seem to multiply more rapidly than they have opportunity to differentiate, so that the stroma becomes more and more cellular until a sarcoma-like appearance results. As the same peculiarity may affect the secondary deposits as well as the primary tumor, some have suspected that both tumors existed in combination, and have suggested the name *sarco-carcinoma*, or *carcino-sarcoma*. But such tumors have been referred to in the section upon "Mixed Tumors," and we are of the opinion that they arise from a primordium of mixed character.

There is a widespread belief that the benign forms of epithelial tumor may "become malignant." Many small adenomas of the breast have been removed "lest they become malignant." It cannot be proven that they do not, nor can it be said that the generally irregular structure and behavior of tumors may not make them more liable to do so than normal tissue, but such transformation must be extremely rare. A few have published histological descriptions of tumors changing from adenoma to carcinoma, but they do not stand the scrutiny of skeptical consideration. It can never be known what the original structure was before the presumed change began; epithelial irregularity is very frequent in adenomas, and seems to be of no prognostic importance. But what is of the greatest importance is that in most of these cases the adenoma is supposed to be transforming into carcinoma, which clinical experience shows it almost never does. When a supposed adenoma of the mammary gland becomes malignant, it is almost invariably through sarcoma of its stroma.

But whether the malignant change be of frequent or rare occurrence, and whether it be with resulting carcinoma or sarcoma, tumors that seem to belong to the class of benign neoplasms do occasionally turn out to be malignant, so that it is undoubtedly good practice to eradicate them.

TUMORS ARISING FROM OR IN CLOSE RELATIONSHIP WITH SQUAMOUS EPITHELIAL COVERED SURFACES

A. Tumor-like Infections of the Skin and Mucous Membranes.
   1. Characterized by upward growth or excrescence.
     Verucca or wart.
     Condyloma acuminatum.
   2. Characterized by circumscribed downward growth into the derma.
     Molluscum contagiosum.
B. Benign Epithelial Tumors—Excrescences.
   Papilloma.
C. Malignant Epithelial Tumors.
   Squamous epithelioma—squamous cell carcinoma, cancroid, carcinoma cutis.

1. Chiefly composed of undifferentiated basal cells.
    Carcinoma basocellulare.
2. Chiefly composed of more or less well differentiated ascanthus cells.
    Carcinoma spinocellulare.
D. Tumors Arising from the Appendages of the Skin.
    1. From the hair follicles.
        Carcinoma trichocellulare.
    2. From the sweat-glands.
        Syringocystadenoma.
    3. From the sebaceous glands.
        Adenoma sebaceum.
E. Tumors Arising from Cells of Uncertain Origin in the Skin.
    Cellular naevi.
    Pigmented naevi.
    Chromatophoroma—melanotic sarcoma.

VERUCCA

Verucca, or warts, comprise small, nodular, filiform, polypoid or sessile neoplasms that occur principally upon the skin of the hands of children. But they may occur anywhere, and at any age, are commonly multiple, and not infrequently occur in crops, small new ones springing up in the neighborhood of older ones. Partly on this account, and partly because some of the older ones have flattened granular surfaces, there is a vulgar impression that the little ones are descendants of the larger ones which are called "seed warts."

They appear mysteriously, grow slowly from small beginnings, sometimes cause considerable pain and annoyance, especially when upon the palms of the hands or soles of the feet, and may unexpectedly and mysteriously disappear.

Investigations carried out by Lanz, Judassohn and Wile have shown the juvenile warts, at least, to be infectious. Inoculation with a filtered extract of a wart, after a fairly definite incubation period, causes the appearance of fresh lesions which remain for some months, and then gradually disappear.

A wart consists of hypertrophic papillae of the skin, covered with considerably thickened epiderm. As its histology does not differ essentially from that of papilloma, further particulars will be reserved until that subject is reached.

The ordinary warts are called *verucca vulgaris;* if they occur upon the skin of the young, *verucca juvenilis.* Multiple flattened lesions sometimes appearing upon the hands, face, scalp, and genitalia of adolescents are particularly described as *verucca plana juvenilis.* They are somewhat more persistent, and may have a different etiology from the others, as may also the *verucca senilis* that occasionally appears upon the skin of the back, chest, upper arms, and face of older persons, as *verucca planus senilis* when flat, and *verucca seborrhoeica* when dry and scaly upon the surface.

CONDYLOMA ACUMINATUM

This is commonly known as the venereal wart, and is a larger and more acute disturbance appearing almost exclusively upon the genitalia of patients suffering from gonorrhoea. Other infections, however, seem to be responsible for similar lesions sometimes occurring in the mouth, in the axilla, about the umbilicus, and between the toes.

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These warts grow rapidly, and are almost always multiple. They form rather soft, nodular, lobulated, digitate, or villous excrescences that bleed freely when injured and usually are covered by an offensive muco-purulent exudate that dries and crusts. Occurring upon the drier parts of the skin they may lack the exudate. The size varies up to a centimeter or more in diameter.

Being infectious in nature, the lesions may disappear with their cause, but they are so annoying that patients usually prefer to have them removed.

In histological structure they do not differ essentially from the verucca and the papilloma.

PAPILLOMA

It is difficult to draw any sharp line of distinction between the wart and the papilloma except that the latter is usually single, larger, and permanent. To casual inspection, a papilloma is a large wart.

FIG. 225.—Papilloma of the tongue. (*Dr. F. D. Weidman.*)

But size does not apply if the papilloma be upon the mucous membranes. A papilloma of the larynx may be no larger than a pin's head, a typical wart upon the hand of a child as large as a hazelnut.

Papillomas of various size and appearance occur upon the skin, and the squamous covered epithelial surfaces of the mouth, the larynx, the cervix uteri, the vagina, the bladder, the pelvis of the kidney.

The size may vary from a pin's head to a small apple. The shape also varies greatly. Upon the skin they may be sessile, pedunculated, fungous or filiform; they are not infrequently lobulated, and may appear rugose or convoluted. Upon the mucous membranes they are apt to be more complex, and are lobulated, villous, arborescent or dendritic.

Upon the skin there is sometimes an exaggeration of the horny layers and not infrequently there are coarse hairs. If such tumors occur in the neighborhood of the facial or other embryonal fissures, a suspicion of greater complexity should be aroused, and the tumor examined to see that it is not a solid dermoid.

In histological structure the verucca, the condyloma and the papilloma consist of a fibro-vascular core arising from and connected with the subcutaneous or submucous tissue, with superimposed stratified epithelium. In the warts the core consists of hypertrophied papillae of the skin, but in the larger tumors it contains more tissue than can be thus explained, and the original papillary structure, if it were the starting point, is effected. The central fibro-vascular core is very slender in the villous tumors of the bladder, and short and thick in the sessile tumors of the skin. Over the former there may be only one or two layers

of epithelial cells, but over the latter there may be dozens. It is the different proportions of fibrillar and epithelial tissue, as well as the variety of squamous epithelium covering the tumors, that give them different shapes and qualities.

In the venereal warts—condyloma acuminatum—the epithelial layer covering the papillae is enormously thick, and the cells having multiplied rapidly, have not completely differentiated. This tends to keep the tissue soft, as does also the associated infection which keeps the vessels full and causes invasion of both
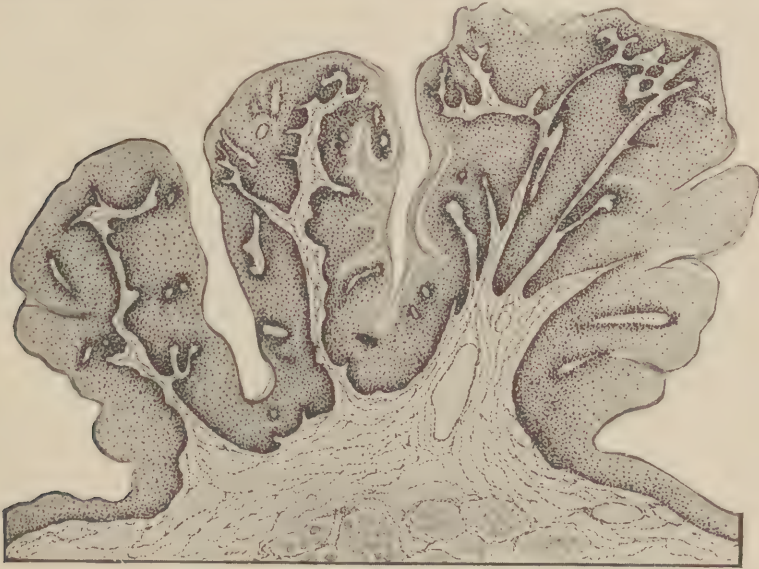
Fig. 226.—Papilloma from the mouth.   (*Bowlby and Andrewes.*)

the connective and epithelial tissues by leukocytes. Infection of all warts is frequent because their exposed position predisposes them to injury, and because of applications frequently made in the hope of getting rid of them.

In the dermal papillomas the complicated papillary structure results in the presence of little pockets which become filled with epithelium. In the natural order of things, the superficial keratinized epidermal cells are desquamated, but in the pockets desquamation is impossible, and the transforming cells become aggregated into small concentric masses showing a varying but usually a high degree of keratinic change, and known as "epithelial pearls" or "pearly bodies."

The fibro-vascular core may be looked upon as an exaggeration of a papilla or group of papillae, sometimes simple, sometimes branched, sometimes slender, sometimes coarse. If a single papilla elongate greatly, but remains slender, a digital or filiform growth may result; if it elongate, but simultaneously broaden, the growth may be sessile, polypoid or fungous. If a group of neighboring papillae simultaneously elongate, a villous tuft may result; if they elongate and broaden, a rounded, lobulated mass results. But the structure and appearance do not depend solely upon the core; the epithelium must be considered. If the elongated and slender papillae be covered by a comparatively thin covering of epithelium, the growth remains villous; if with immensely thickened epithelium,

it may appear lobulated. If the villous, lobulated or dendritic growths become amalgamated through contact and blending of the growing cellular coverings or if they be held together by some sticky material such as mucus or fibrin, as may happen upon the mucous membranes, a rounded, nodular, solid appearing mass is formed.

The structure is simple and typical. Nowhere is there any disorder of arrangement, and nowhere any invasion of the subjacent tissues by the epithelial cells; all grow upward, and as far as local conditions permit, fulfil their normal transitions. Cells of the skin pass in regular succession through the basal to the intermediate layers with the acanthous or pickle cells, then on to the outer horny layer. In the recess between the villi or lobulations, or beneath the overhanging borders of the fungous growths, the horny cells collect as concentric laminated pearly bodies, which though often very large are not very numerous as a rule. In papillomas of the bladder and renal pelvis there may be no pearly bodies, though there are analogous concentric formations of much smaller size lacking the keratinic quality.

Villous papillomas of the bladder may appear to be composed of spindle cells in many layers, radiating from the central core, and fraying out at the surface, where the flattened cells have been lost.

Verucca, condyloma acuminatum and papilloma are all benign tumors. Occasionally warts recur when excised, but that is probably because some of the infectious agents remain. Warts and papillomas of many years standing have, in rare cases been known suddenly to take on invasive and malignant growth, and eventually destroy the patient.

Exactly what this signifies is not clear. When the malignancy is manifest it is too late to determine how the particular tumor differed from others that did not so misbehave.

Molluscum Contagiosum

Molluscum contagiosum is an infectious disease of the skin with tumor resemblances that make it perplexing to those not familiar with it, and who may receive it from the clinic or dispensary where large lesions are sometimes excised under the misapprehension that they are beginning basal cell carcinomas.

Fig. 227.—Typical lesions of molluscum contagiosum upon the face of a little girl. (*Dr. F. D. Weidman.*)

These lesions may be single or multiple, are occasionally very numerous and sometimes may be observed to occur in successive crops. They are usually small, commonly not larger than a pin-head or a pea, but may reach the size of an orange. They are most frequently situated upon the skin of the face and genitalia, but may occur almost anywhere, and have been observed upon the mucous membrane of the mouth. In a considerable sized epidemic reported by Hartzell, the lesions were present in large numbers, were chiefly situated upon the trunk, and frequently occurred in lines corresponding to scratches. They were supposed to be the result of infection by bath-towels.

Each lesion resembles a small smooth wart, the color of the normal skin, and is usually embedded or sessile, but in rare cases may be pedunculated.

Sooner or later each acquires a central umbilication in which there is a small opening. The lesions are solid, painless, and insensitive, unless inflamed as the result of secondary infection, when they may itch and become red and tender.
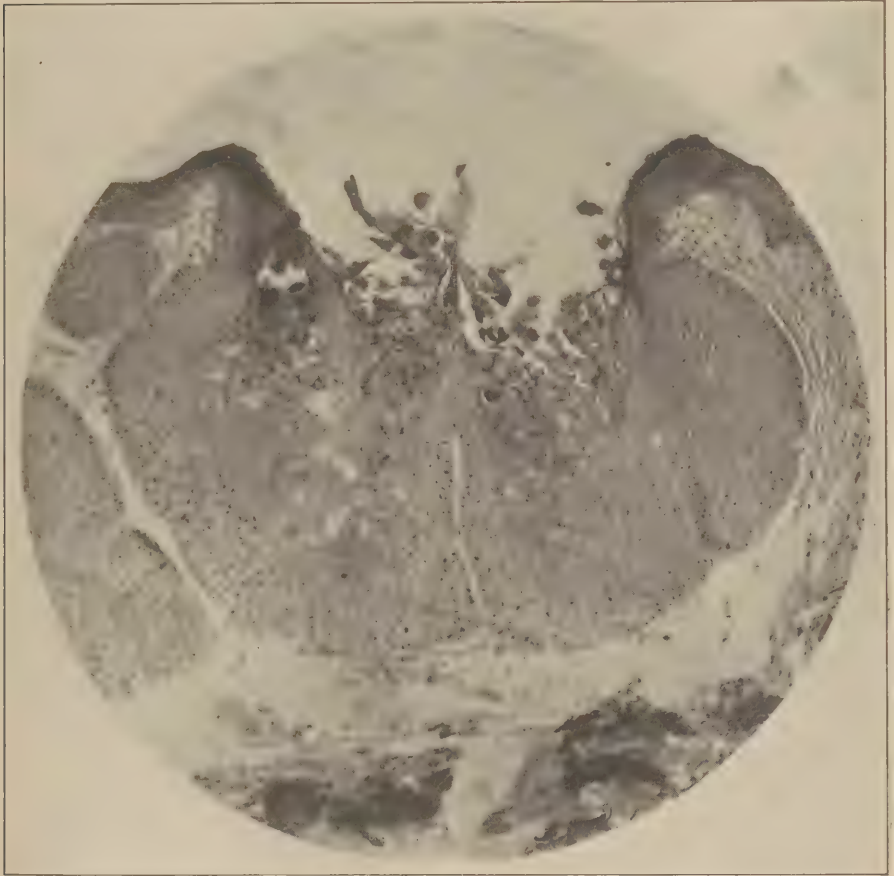
FIG. 228.—Microscopic section of a typical lesion of molluscum contagiosum showing the typical " molluscum bodies " escaping into the central umbilication which forms the excavation at the top of the illustration. (*Photomicrograph by Dr. F. D. Weidman.*)

They continue without much change for months or even for years, but eventually disappear spontaneously, especially if infected.

Inoculation experiments carried out by Retzius, Pautry, Haab and Pick show incontrovertibly that molluscum contagioum is an infectious disease, and Juliusberg has discovered that the virus is filterable. Infection may be direct or indirect.

The histological structure is perfectly characteristic. Each lesion consists of a lobulated mass of epithelium which seems to arise through multiplication of the epithelial pegs of the rete, until a spheroidal cellular mass is formed by the

amalgamation of several.   The whole is definitely circumscribed by a kind of capsule of fibrillar tissue, some of which was probably preexistent, some newly formed; the lobules are separated from one another by prolongations of this same tissue.

The multiplication of the cells elevates the suprajacent epiderm which degenerates and disappears leaving the central umbilication and opening.   The proliferation affects the basal cells principally, hence the lesion sufficiently resembles basal cell carcinoma to confuse those not familiar with it.   But the cells undergo a peculiar degeneration immediately below the central opening, resulting in the appearance of what are known as "molluscum bodies" that are diagnostic, and so peculiar in appearance that Darier mistook them for parasites and described them as "*psorosperms*."

Ewing describes the cell degeneration in these words: "The cytoreticulum becomes thickened and coarse at the expense of material from the nucleus, and a large portion of the cytoplasm thus becomes converted into a well-defined reticulated substance imperfectly separated from the nucleus and cell membrane and appearing as a foreign body.   The nucleus eventually shrinks to one side of the cell.   The variations in the minute structure of these molluscum bodies are quite numerous."

Hartzell found that three varieties of degenerated cells might be distinguished: "First and most numerous, large round bodies with doubly contoured walls and granular segmented contents in which the nucleus is excentric, much dilated, and frequently flattened out against the inner wall of the cell; second, oval cells lying in the midst of normal epithelium, with thick laminated walls, filled with a felt-like mass of fine short fibres and with a nucleus lying in a cavity at one pole of the cell; and third, completely degenerated cells which appear as oval, deeply stained, structureless bodies."   He also observed a previously described form in which "the cells were smaller than those described above, perfectly oval in shape, had a double wall, were filled with a mass of fine fibrils, and were without nuclei."

The nature of the cell degeneration has not been determined; some think it hyaline, others colloid, still others keratinic.

Squamous Cell Carcinoma; Squamous Epithelioma

This malignant tumor is supposed to arise through downward, irregular, and unlimited growth of the squamous epithelium, followed by invasion and destruction of the subjacent structures and metastasis to the lymphatic nodes.   How it begins is not definitely known, for it cannot be recognized, as such, until it has existed for a certain time.   By that time, although it may still be very small, its actual beginning is obscured.   But the study of very small tumors, and the margins of larger ones, have led to the generally accepted theory that the tumor has its origin in the downward growth of the epithelial pegs of the epiderm.   If the line of the normal epiderm be followed to the edge of the tumor, and then as far as possible on to the surface of the tumor itself, these pegs may be observed to become larger and larger, and more complex, with such regularity that it is sometimes impossible to say where the normal tissue ends and the tumor begins.

Ribbert supposes that it is not from the normal epiderm that the tumor originates, but from some of its cells that have become separated and sequestered in the deeper structures as the result of inflammatory or other antecedent morbid conditions. Disciples of Cohnheim attribute it to the growth of residual embryonal cells, situated either among the cells of the adult epiderm, or in close juxtaposition to it.

That the adjacent epithelial pegs of the epiderm enlarge as the tumor is approached ought not to be given too much weight as indicating that the tumor arises from them, for the enlargement may indicate nothing more than irritation about the borders of the tumor, with resulting hypertrophy of the papillae and pegs of epiderm.

The disease, however, sometimes follows chronic irritation of the skin in lupus vulgaris, syphilitic lesions, old scars, etc. It sometimes seems to start at the irritated bases of warts, horns, and open sebaceous cysts. The scaly patches upon the skins of the aged occasionally "become epitheliomatous." Some cases can be referred to the chemical irritation of soot, as in "chimney sweep's cancer," and coal tar and paraffine. Upon the lips, the combustion products in the stem of a clay pipe appear to initiate the disease, and in the mouth it frequently starts in an ulceration caused by a sharp carious tooth. At the cervix of the uterus it is commonly a laceration following child birth.

As the multiplication of the stratified epithelia is largely restricted to the cells of the basal layers, it is supposedly from them that the tumor arises. Its subsequent varying appearances depend in large measure upon the natural transformations of the particular epithelium concerned, and the success of its cells in fulfilling them. If the basal cells multiply without transformation, a tumor follows that is characterized by masses of similar appearing cells—carcinoma basocellulare; if they multiply and transform into prickle and kerantinized cells —carcinoma spinocellulare.

But this method of accounting for Krompecher's carcinoma basocellulare is not satisfactory to all pathologists, and Mallory says that "the idea which has been advanced and which has obtained wide notoriety, that a carcinoma starting from the rete Malpighii does not undergo cornification, is absurd." He believes "that there are better explanations for the origin of the tumor" and considers that it develops from the cells of the hair matrix. That tissue, however, seems to be the starting point of a different tumor later to be described as carcinoma trichocellulare. We see no valid reason, at present, for differing from Krompecher.

Carcinoma Basocellulare

This form of skin cancer is also sometimes called tubular epithelioma, epithelioma exedens, Jacob's ulcer, and above all *rodent ulcer*. Broders found it forming 13.4 % of 2000 cases of skin cancers studied, the average age of the patients being 56.7 years.

It is most common upon the faces of adults past the meridian of life.

The points of most frequent occurrence are the cheeks, eyelids, nose and forehead. Similar tumors also occur, though rarely, upon the trunk, genitalia

and extremities. They also occur upon the mucous membranes, but are much less characteristic because of the general indisposition of the epithelium of those structures to differentiate, and their general greater resemblance to the basal cells.

FIG. 229.—Carcinoma basocellulare of the upper lip.

FIG. 230.—Carcinoma basocellulare of the upper lip and cheek.

In its first appearance the tumor may form an elevated, fairly well circumscribed whitish nodule, or be preceded by a scaly patch upon the skin, and the tumor is first recognized as a flat tabular swelling which early ulcerates and
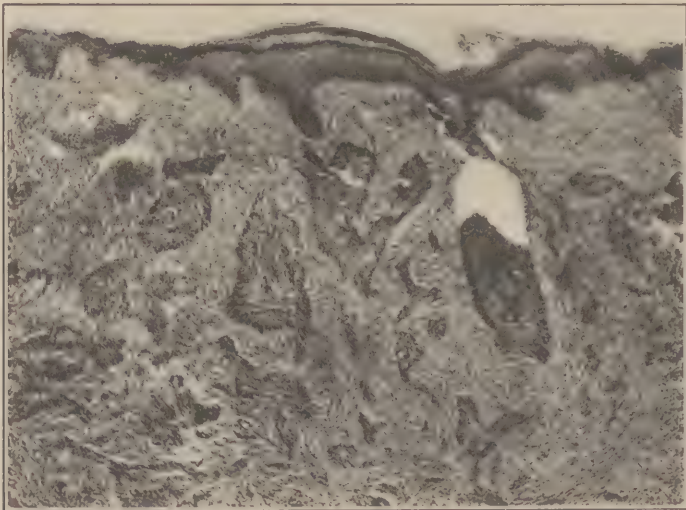
FIG. 231.—Microscopic section of a very young carcinoma basocellulare, with collections of spindle-shaped cells. (*Photomicrograph by Dr. F. D. Weidman.*)

slowly and persistently extends. The lesion is extremely indolent in most cases, and its surface becomes covered by a crust that is dry and brown, but beneath which no healing takes place. If the crust becomes detached a new and larger one forms, and thus the tumor slowly grows, unless its surface becomes

infected when it may become more active and more moist. The indolence of the lesion is well shown in the case of a tumor of the forehead that came under our observation. It had required more than 30 years to reach a diameter of 5 centimeters.

Sometimes, however, much greater destruction is effected in a few years. Growth may be regular, or by fits and starts. The ulcer is reddish, glazed, and surrounded by a purplish, indurated, but not considerably elevated border. It is usually superficial, but various depths are attained; usually it is fairly

FIG. 232.—Microscopic section of a well-developed carcinoma basocellulare, showing the large masses of cells, many of which are small, crowded closely together, and of spindle shape. (*Photomicrograph by Dr. F. D. Weidman.*)

limited to the skin, but it may go more deeply and erode the bones as well as the cartilages of the nose and ears. Most patients die of intercurrent affections.

In rare cases the ulceration does not occur until there is a well-developed tumor. Recently there came under observation a well-circumscribed solid tumor of the scalp about the size and shape of a lima bean. It was not ulcerated, and had caused no symptoms. The microscopic structure brought it into line with tumors of this class.

Small tumors removed with considerable of the surrounding skin may not return, but experience shows that most of them do. Small tumors may be destroyed with arsenical paste, but then may return and grow more rapidly. Fulguration with the electric spark is sometimes employed when the tumors are small. Exposure to X-rays, and especially radium, cures a large number. There is usually ample time for repeated treatments, if needed, as not only does the tumor grow slowly, but it shows no disposition to give metastasis, either locally or generally.

Krompecher described basal cell carcinomas arising from the lowest layers as composed of columnar cells, those from cells higher up of cuboidal cells, but in many cases the cells appear to be distinctly spindle shaped. The cells either grow in great aggregations, more or less rounded in form, which lie in the cutis without infiltrating the adjacent structures; or they form a closely compacted complicated series of branching processes.

Students are usually taught that the most significant diagnostic feature of the carcinomatous tumors is the loss of the definite relationship between the cells and the basement membrane. This does not at all apply to the basal cell carcinoma, for almost everywhere the cells stand in orderly arrangement upon the basement membrane. It is probably partly on account of this preserved relationship that the tumor is so slowly invasive and so free from metastasis.

The large size of the cell clusters, combined with the occasional spindle shape of the cells, and absence of the transformations expected of epithelium, sometimes make it a question whether a given tumor is not a sarcoma. But knowledge of the seat of the disease and of its history ought, at once, to enable sarcoma to be ruled out.

The larger cell masses are sometimes riddled with small spaces resulting from the degeneration of the cells, and the branching, ramifying prolongations are frequently hollowed out by vacuolation and degeneration of the cells. It is probably on this account that the tumor sometimes is called *tubular epithelioma*. But this tubular appearance has been otherwise interpreted, and some have thought the spaces to be lymphatics, whose lining cells were the starting point of the tumor growth, and have regarded the basal cell carcinoma as a variety of endothelioma.

There are no prickle cells, and never any epithelial pearls, or other signs of keratinization in typical basal cell carcinoma.

Between the epithelial masses and the tubular prolongation there is a fibro-vascular stroma composed of little more than the antecedent corium with its capillaries.

Between the tumor described and the next following there are intermediates of every grade. It would be a serious mistake to suppose that because only two varieties, the basal cell and the prickle cell tumors, have been given distinctive names, all carcinomas of the skin and squamous mucous membranes must fall into one or the other. There are as many intermediate non-de-script forms as there are typical representatives of either of the named classes. If it seems necessary to find a special name for these, they might be called "indeterminate squamous cell carcinomas." In prognosis they more closely approach

the malignancy of the carcinoma spinocellulare than the comparative benignancy of the carcinoma basocellulare, and they do not yield as readily as the latter to the destructive and curative influence of X-rays and radium.

FIG. 233.—Senile horny wart of forehead, from a woman eighty-four years of age. *a* Corium; *b*, epithelium; *c*, atrophic sebaceous glands, with development of horny epithelium in their ducts; *d*, hypertrophic horny layers; *e*, enlarged papillae.   ×15.   (*Ziegler.*)
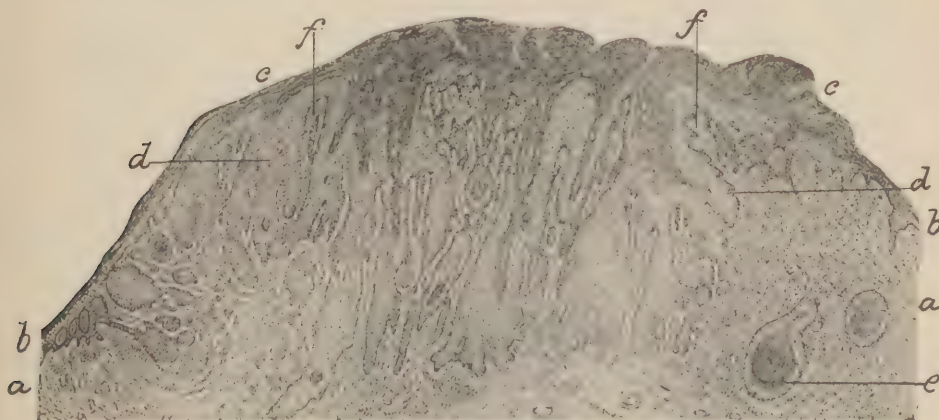
FIG. 234.—Transverse section through a squamous-cell carcinoma of the lip—alcohol, haematoxylin, eosin.   *a*, Corium in a state of proliferation; *b*, epithelium; *c*, thickened horny layer; *d*, epithelial plugs extending into the corium; *e*, epithelial plugs with horny pearls, cut obliquely; *f*, enlarged papillae.   ×12.   (*Ziegler.*)

Carcinoma Spinocellulare

This variety of carcinoma, principally arising in the skin, is characterized by the disposition of the multiplying cells to complete their natural differentiations, and pass through the stage of prickle cells to that of keratinization.   In many

cases the tendency to keratinization is excessive, and may show itself where, under normal conditions, no such change is expected, as, for example, in tumors arising from the mucous membranes.

In some cases the prickle cells are present in great abundance —carcinoma spinocellulare—in others the keratin formation is greatly exaggerated—carcinoma keratoides. There seems to be little reason for making this distinction, however, for the two usually go hand in hand.

FIG. 235.—Squamous-cell carcinoma. a, Epithelial masses; b, epithelial pearls; c, connective tissue; d, capillary blood vessels.

Carcinoma spinocellulare may occur upon any of the squamous epithelial covered surfaces. It occasionally arises where squamous epithelium is not normally present—the gall-bladder, body of the uterus, intestine, stomach, nasal fossae, and bronchi.

In these cases it may be the result of embryonal epithelial cell inclusion, or may possibly be the result of metaplasia. The former seems more probable as such tumors occasionally occur from embryonal vestiges of the branchial grooves in the lateral aspects of the neck. In rare cases squamous cell carcinomas have been observed in dermoid cysts.

The distribution of the tumors is very wide, and they are extremely common. Our collection of cases shows them from the anus, axilla, cheek, eye-lid, conjunctiva, cornea, bladder, cervix uteri, face, hand, jaw, leg, lip, mammary areola, neck, nail matrix, mouth, nose, palate, tonsil, tongue, thigh, penis, scrotum, vulva, esophagus, renal pelvis, body of the uterus, and gall-bladder.
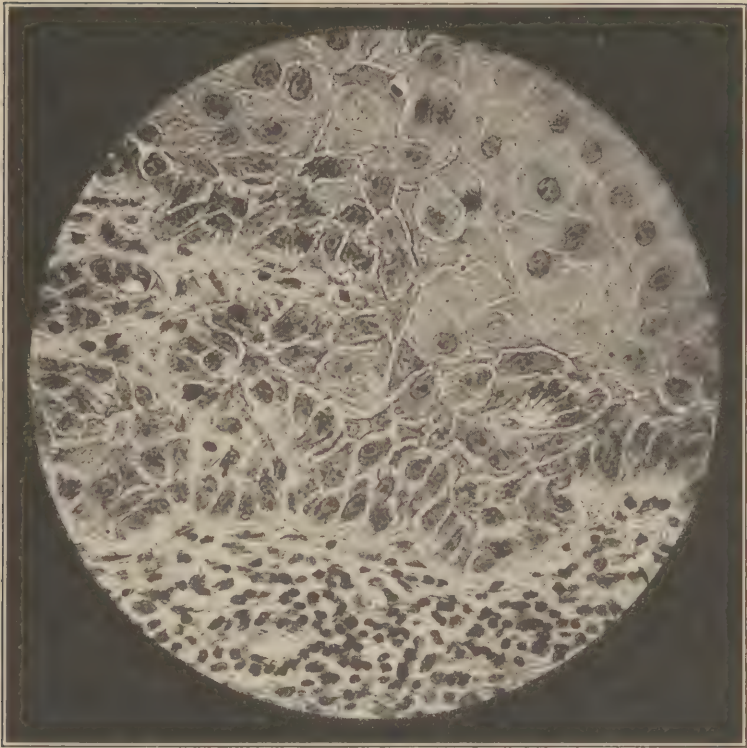
Fig. 236.—Microscopic section of part of a carcinoma spinocellulare, showing the acanthous or prickle cells above and to the right. (*Photomicrograph by Dr. F. D. Weidman.*)

Fig. 237.—Epithelioma spinocellulare of skin. (*Matas.*)

They are usually solitary, but multiple primary tumors of this kind are not uncommon, especially when caused by soot, tar, paraffine, or burns.

There are two chief clinical morphological varieties, the *superficial papillary* and the *deep ulcerative;* but there are many intermediate non-classifiable varieties as well.

The clinical appearance varies greatly according to the position, the type, and the age of the lesions. In general, however they are all characterized by slow formation, superficial ulceration, and extending infiltration. It is by the painless slow onset that the lesion is to be differentiated from benign inflammation. There are no infallible means for clinically differentiating it from chancre or other syphilitic lesions.

The superficial ulceration varies in depth in different cases, and is usually covered with necrotic material that tends to crust. In the course of time the loss of tissue from the ulceration may be great, and productive of hideous deformity; whole lips or cheeks being destroyed, or an orbital cavity excavated and the bones exposed.

FIG. 238.—Carcinoma spino-cellulare of the lower lip.

When studied histologically, the tumor is found to be made up of a complicated system of extending, ramifying, epithelial processes, connected together like roots of a plant, descending into the corium and subcutis which are penetrated in all directions. In sections some of these are cut longitudinally, some obliquely, some transversely. The longitudinal sections enable one to see the connections between the various parts, though to study them to advantage, serial sections are necessary. The transverse sections appear as disconnected groups of cells surrounded by connective tissue. The impression that the whole thing has descended from one or more of the suprajacent epithelial pegs is justified, if not correct. In some places the epithelial processes are blunt and rounded, and the cells regularly arranged both with respect to one another and to the basement membrane. In other places, however, they appear as long slender columns in which the cells are more or less disconnected, and which terminate in detached single cells that infiltrate the surrounding tissue without reference to any boundaries. When the arrangement is regular, it can be seen that the outer cells of each process correspond to the basal cells, and the more internal to the prickle cells, while in the very interior, corresponding to the most superficial of the cells of the epiderm, keratinization can be seen, commonly taking the form of epithelial pearls, some small, some large.

These pearly bodies are almost as diagnostic of carcinoma spinocellulare as the prickle cells themselves, and are sometimes present in great numbers, though of small size, sometimes in small numbers and of large size. In addition to the pearls, or sometimes in their place, may be irregular keratin masses, or scattered clumps of keratin, corresponding to transformed single cells. In tumors of the mucous membranes, there may be whorls of cells not keratinized,

but in formation corresponding to the pearls. Occasionally these show a slight keratin formation. The keratin is usually colorless in the unstained tissue, and pinkish in that stained with eosin; sometimes it is yellowish, and remains so. Where scattered keratin occurs, there may be occasional foreign body giant cells, apparently attempting its removal.
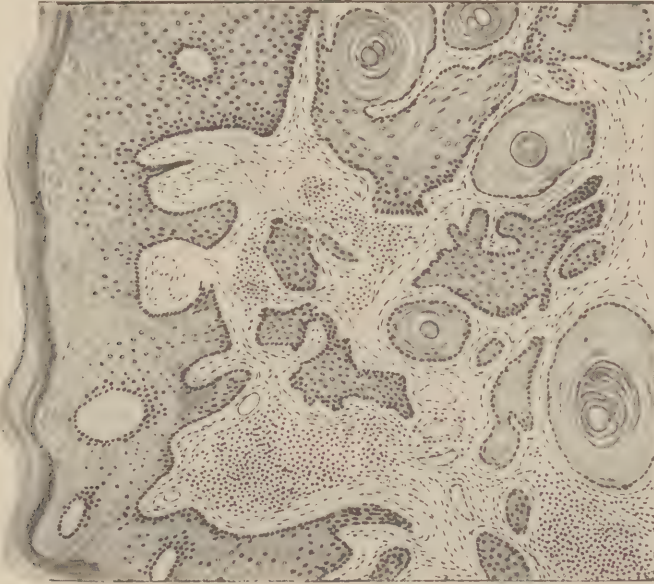
FIG. 239.—Carcinoma spinocellulare from the skin, showing epithelial invasion of the deeper tissues and the presence of numerous epithelial cell nests (pearls). There is an inflammatory exudation in the adjacent tissues. (*Bowlby and Andrewes.*)

Not infrequently there are lymphocytes or leukocytes in small numbers among or in the cells of the pearl. What they signify is not known.

Occasionally the epithelial pearls calcify. This seems to be a peculiarity of the tumor, and not of the pearl.

Many of the cells in the larger groups become so far removed from the source of nutrient supply that the intercellular lymph conveyed through the canaliculi between the prickles is no longer sufficient to sustain them. They then undergo necrosis, which is soon followed by ulceration.

With this accident comes almost inevitable infection, more or less infiltration by leukocytes, lymphocytes and plasma cells, and more or less edema of the connective tissue. Additional nutrition is then supplied to the surviving peripheral cells and the tumor grows faster; the epithelial cells become dislocated, and there is an increased tendency to metastasis, as well as to local invasion and destruction. Very severe infection as by streptococci, followed by erysipelas, has been known to effect the complete destruction of the tumor, which disappeared, never to return.

Leukocytes that have eroded their way into the cells, or are present in them as the result of phagocytosis, rounded bits of keratin, vacuoles of unknown

origin, and epithelial cells seeming to be included in other cells, form a variety of cell inclusions, readily mistaken for parasites.

The long branched, cellular processes with their cell strands and detached cells explains the early metastasis to the lymph-nodes by which this tumor differs from the basal cell variety.

Careful surgeons now remove the regional lymph-node when operating upon primary squamous cell carcinoma of the lip or tongue, in which tumors experience shows early metastasis to be the rule. When that is done, the patient more frequently escapes return than when the tumor only is removed.

The secondary tumors in the lymph-nodes or in the lung have, for the most part, the same general appearances as the parent tumor. But in some cases the cells are so anaplastic as no longer to be easily recognizable as descendants of the squamous epithelium. In a metastatic tumor of the inguinal node of a patient whose penis and scrotum had some time before been removed for squamous cell carcinoma, the cells were of many sizes and shapes, were not definitely arranged in groups or formed into processes, and among them were great numbers of enormous cells with large nuclei and deformed mitoses, and a great number of small and large giant cells, some of which had a vast quantity of protoplasm in proportion to the number of nuclei. With no knowledge of the case, it is doubtful whether a correct diagnosis could have been reached.

Some cases, especially of young tumors, can be successfully treated by electric spark fulguration, and by X-rays and radium.

Carcinoma Trichocellulare

This little tumor is also called *benign cystic epithelioma, epithelioma adenoides cysticum*, and *trichoepithelioma papulosum multiplex*. It is the most benign of the group of "epitheliomas," and seems to be derived from the cells of the hair follicles, as was first suggested by Jarisch. But it is still regarded by some (Mallory) as identical with carcinoma basocellulare, and supposed to have the same origin. As will be seen, however, its clinical manifestations are quite different and characteristic.

It nearly always appears upon the face, usually in the neighborhood of the temple, forehead, eyelid, root of the nose, and more rarely upon the lower part of the face, the lips and chin. Very rarely only does it occur upon the trunk.

The lesions are nearly always multiple, and are rarely larger than a pea. They are also about the color of the normal skin, though sometimes yellowish or pinkish. They are translucent, and may be mistaken for vesicles—milia, —but when they are punctured, are always solid. They first appear in childhood or youth, and have a disposition to occur in groups, which may develop one after another. Slowly increasing to about the size of hemp seeds or peas, they remain indefinitely without healing, yet showing no inclination to spread, and rarely ulcerating. The course is thus benign. The little tumor does not return when excised, and never causes metastasis.

Histological sections show the tumors to be composed of rounded or branched masses of epithelial cells situated in the corium, with scarcely any disturbance

of the epiderm. The outer cells have a columnar shape, as in the basal cell tumor, and are arranged radially in palisade formation. But the centers of most of them degenerate, and give rise to cystic spaces filled with fluid and cell remnants. In some cases the tumor cell masses can apparently be traced from the epithelial pegs, but Hartzell thinks that in such cases the tumor has

FIG. 240.—Microscopic section through a small and young carcinoma trichocellulare, with cells in narrow strands, some of which seemed to connect with hair follicles. (*Photomicrograph by Dr. F. D. Weidman.*)

grown up to the derm, and not the derm down to the tumor. Serial sections are said to show connections between the cell masses of the tumor and those of the hair follicles.

These little tumors usually respond to simple modes of treatment. Many can be destroyed by application of solid carbon dioxide; they all quickly disappear under the application of X-rays or radium.

Syringocystadenoma

This rare little tumor was first described by Jacquet and Darrier, in 1887, but its actual nature and origin are still much in dispute. At first it was supposed to arise from the sweat glands, but Jacquet later came to regard it as

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identical with the benign cystic epithelioma, and Hartzell supports him in that view. But it differs clinically from benign cystic epithelioma in appearing by preference upon the upper anterior surface of the trunk and inner surface of the arms, in the form of a number of discrete papules and minute nodules of pinhead and half pea size. They are slightly elevated, flattened, yellowish, pinkish or brownish in color. Though there may be many of them they usually give rise to no subjective symptoms, and may remain for years without change.
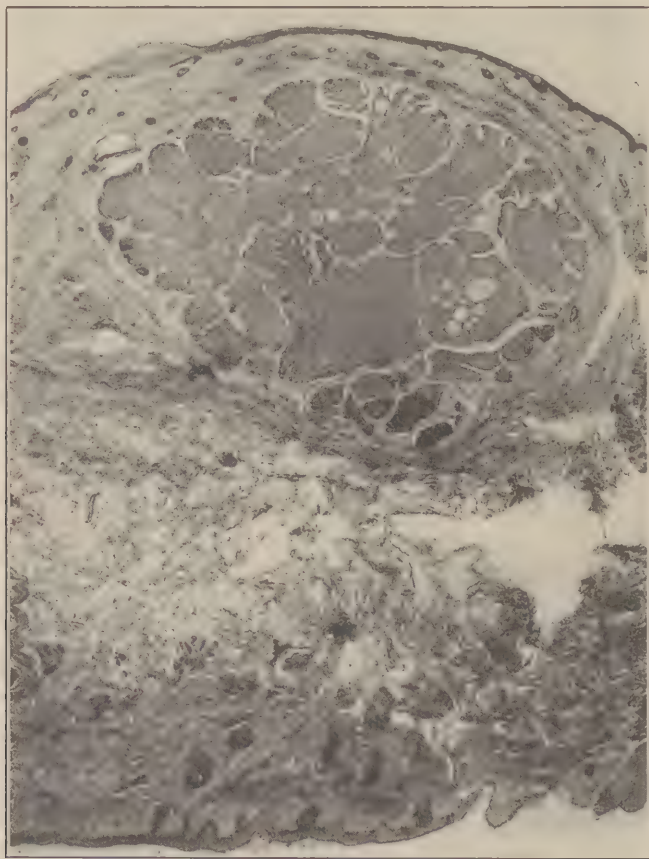
Fig. 241.—Microscopic section through an entire carcinoma adenoides cysticum (benign cystic epithelioma) of the eye-lid. (*Photomicrograph by Prof. Allen J. Smith.*)

Hartzell's sections of these tumors showed them to be composed of numerous straight or branching slender tracts of columnar epithelium situated in the corium, together with a number of round and oval cysts lined with laminated epithelium, and filled with hyaline material.

The epithelial tracts are quite narrow, usually not more than two or three rows of cells in width, recalling the appearance of the coil glands, but without their lumen. The cysts, which are frequently of considerable size, are sometimes connected with the epithelial tracts; occasionally they are situated within

the follicles. In some cases he could trace a slender, duct-like tract of epithelium to the lanugo follicles, and thus establish origin from their lateral spurs.

Some authors, Jarisch and Walters, look upon this tumor as an endothelioma originating from the blood-vessels, and Grossmann and Winkler regard it as a variety of naevus.

In a case reported by Hollopeau, the lesion upon the eyelid of the patient, had been present from childhood. He became a man before it became malignant.

Adenoma Sebaceum

Small rounded reddish or yellowish elevations of hemp seed or pea size sometimes occur singly or in clusters about the alae nasi, more rarely upon other parts of the face and still more rarely upon the trunk. When examined microscopically, they are found to be composed of an enormous increase in the number and complexity of the sebaceous glands. They are not tumors, but hypertrophies of the glands, and are harmless, though unsightly. A case of rhinophyma that came under our observation depended upon this cause. They usually persist but have been observed to disappear spontaneously. They are easily destroyed by electrolysis.

TUMORS ARISING FROM, OR IN CLOSE RELATIONSHIP WITH, THE COLUMNAR EPITHELIUM

A. Pseudo-tumors or Hypertrophies.
    (a) From defective regeneration after ulceration.
        Certain polypi of the intestine.
    (b) From chronic catarrhal inflammation.
        Polypi of the nose, stomach, intestine, uterus, etc.
    (c) From bilharziosis of the intestine.
    (d) From coccidiosis of the intestine and liver.
B. Benign Epithelial Tumors.
    I. Characterized by upward, outward growth and the formation of an excrescence.
        Papilloma, i.e., soft papilloma.
    II. Characterized by nodular formations of typical arrangement, in organs.
        Adenoma.
C. Malignant Epithelial Tumors.
    Characterized by downward invasive and destructive growth.
      Columnar celled carcinoma.
        Cylindrical epithelioma.
        Destructive adenoma.

Mucous Polypi

Papillomatoid growths, or pseudo-tumors, are of frequent occurrence upon the mucous membranes where they assume the polypoid and commonly pedunculated form commonly known as *polypi*. They bear the same general relation to columnar epithelial covered surfaces that hard papilloma and condyloma acuminatum do to the squamous covered surfaces, and have ceased to be regarded as tumors because their inflammatory origin is so generally admitted. They sometimes result from excessive regenerative activity, at the borders of healed dysenteric ulcerations of the colon, or other similar lesions.

More frequently they depend upon more distributed irritation, when they are usually multiple, as in polypoid gastritis and endometritis.
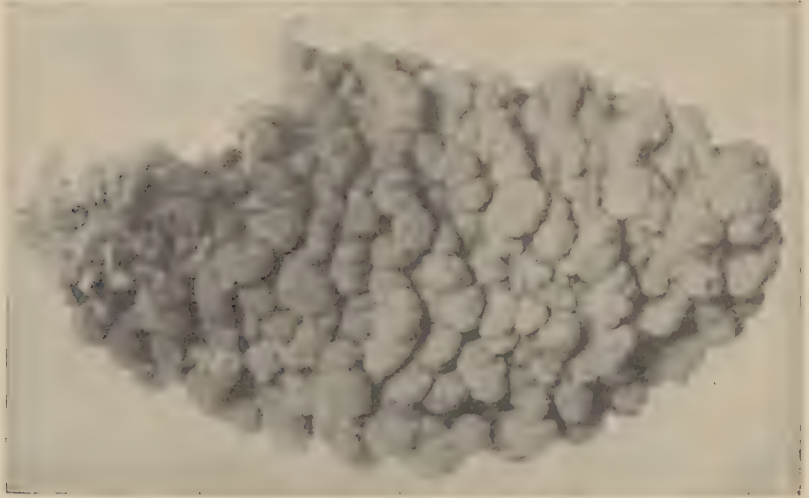
FIG. 242.—Polyposis ventriculi, showing a remarkable number of polypi. (*Eusterman and Senty.*)

FIG. 243.—Marked polypoid growth of colon, approximately actual size. (*Carroll.*)

They vary in size, according to the location in which they occur, from a pea to a small apple, and may be sessile, fungous, or polypoid and pedunculated. In the latter case they may have long pedicles. Their consistence is usually soft, the color red, and they bleed readily upon rough handling.

When sectioned and examined microscopically their structure so nearly corresponds with that of the soft papilloma, later to be described, that it may be impossible to differentiate them unless the source and history be known. Each consists of a central core of fibro-vascular tissue covered with mucous membrane normal to the part, and filled with its glands.

They are to be looked upon as benign hyperplasias, slowly arising as the result of irritation, and probably as slowly disappearing when the cause no longer exists. But about their spontaneous disappearance too little is known to enable any positive statements to be made.

PROTOZOAN INFECTIONS

Coccidial infection of the liver and intestine of young rabbits is very common, and sometimes occurs unexpectedly in children, so that the pathologist should be familiar with it, and not mistake it for a cystic tumor or an adenoma, as has been done.

The disease is caused by a protozoan parasite, a sporozoan, the Coccidium cuniculi, whose spores, being swallowed with green vegetable foods, are opened by the solvent action of the gastric and pancreatic juices, each liberating two small ameboid embryos that proceed to enter the columnar epithelial cells

FIG. 244.—Part of a rectum showing multiple glandular polypi. (*Bowlby and Andrewes.*)

of the intestinal mucosa, or, finding their way into the bile ducts, enter the columnar or cuboidal cells.

In the cells the organism grows to maturity, and becomes a gametocyte. From the smaller of these are eventually liberated a number of spermatozoits by which the larger (makrogamete) is fertilized. After fertilization the organism either divides into a number of banana-shaped merozoits with the same power of invading the neighboring cells shown by the original spore from outside, and by which an ever increasing number of epithelial cells are affected, or encysts itself with a double capsule, passing out of the body with the intestinal contents, to be distributed to new hosts, in whose body it begins the affection as in the first instance.

The result of the intestinal infection is an enormous increase in the size of the infected villi which resemble small polyps, and the appearance in the liver of a group of cystic spaces—coccidial cysts—formed through the dilatation of the affected bile ducts. When one of the latter is examined it is found to be

dilated because of accumulations of debris consisting of desquamated and degenerated epithelial cells, amorphous matter probably derived from them, and great numbers of the parasites in the various stages of development described. But what is of chief interest is the condition of the walls of the bile ducts which are thrown into primary and secondary rougae, sections of which appear much like polypoid excrescences, and have sometimes given the impression that the cell lesion was a new growth, and akin to tumor. It seems, however, to be nothing more than an inflammatory hyperplasia. With the survival of the rabbit, or of the child, the infection eventually wanes, the parasites die out, and the hyperplasia disappears, the position of the former cysts being marked by some increase of the connective tissue.

Vermicular Infestation

Bilharziosis or *Schistosomiasis* is a disease brought about by a trematode worm, the adults of which live in a state of cohabitation in the vessels of the intestine or bladder. From the body of the female eggs are discharged into the vessels and accumulate in the capillaries, spines with which they are provided preventing them from being swept along by the circulating blood. The masses of eggs effect obstruction with resulting ulcerations from which the eggs escape either into the intestinal contents or into the urine, and so leave the body. The prolonged irritation effected by the presence of the eggs induces hyperplastic changes with polyposis and indurations appearing much like tumors and, sometimes, it is said, actually eventuating in carcinoma.

Soft Papilloma

This tumor, appearing upon surfaces covered with columnar epithelium, corresponds with the hard papilloma of those covered with squamous epithelium. It occurs in the nose, uterus, Fallopian tubes, biliary ducts, stomach, intestine, ducts of the mammary gland, in mammary and ovarian cysts, and upon the choroid plexuses of the brain.

The tumor is comparatively rare except in ovarian cysts, where it seems to reach its maximum development.

In its most typical form, the soft papilloma resolves itself into an arborescent excrescence, the central stalk of which corresponds to the trunk of a tree, the general mass to its complex branchings. The color is usually red, the consistence soft. Mucous and amorphus matter frequently collect in the spaces between the branches, or spread upon the surface, sometimes making it appear like a solid tumor with a smooth surface. Putrefaction of this material also sometimes gives it an offensive character, and there is usually considerable discharge which may be bloody.

The tumor varies in size from a pin's head to a man's fist. Its delicate structure makes it fragile, and fragments frequently break off, and in rare cases, especially where the pedicle is slender, the whole tumor may become divulsed.

The smoother the surface from which it arises the more simple and rounded the growth. Upon the uterine and nasal mucosa, the surface is so smooth and the tumor so little divided that it appears fairly solid, and is not infrequently described as an adenoma. Upon the intestine where there are many villi it is most arborescent.

FIG. 245.—Section of a small soft papilloma of the intestine. (*Photographed under a low power to show the whole tumor, by Prof. Allen J. Smith.*)

If a soft papilloma be cut directly through the middle and subjected to histological examination, it is usually found to consist of a delicate fibro-vascular framework, branching more and more towards the surface, until only a few fibres support the blood and lymph-vessels, and form the foundation upon which the columnar epithelial cells rest in single layer and regular formation, perfectly corresponding with the arrangement of the normal tissue from which the tumor arises. The cells usually appear to be in good health, and perform their usual function of mucin secretion, many of them commonly being of the goblet shape. There seems to be no reason for thinking that the glands included in the structure do not also secrete as the corresponding normal glands do.

In the less striking, more rounded tumors of the uterus and nose, there is considerable increase in the fibro-vascular supporting tissue, relatively less of the epithelium, and not so many glands.

Adami supposes that the multiplication of the epithelium is the essential cause of the growth, but the frequent preponderance of the connective tissue foundation of the tumor seems to make this uncertain.

French pathologists speak of these tumors as adenomas, because of the number and complexity of the glandular elements they contain. With this view we are not in sympathy, as will be understood after the perusal of the section upon adenoma.

Papilloma is a superficial growth, taking the form of an excrescence, and is normally unaccompanied by invasion or infiltration of the subjacent tissue. It

FIG. 246.—Microscopic section through the papilloma of the intestine.

is, therefore, a benign tumor, and can be removed with reasonable assurance that it will not return. Or, if it becomes spontaneously divulsed, recurrence need not be feared. But sometimes recurrence does take place, either because the original cause of the tumor growth remains, or because the excrescence is only an external manifestation of a more deeply seated malignant tumor. In both of these respects it resembles the hard papilloma of the squamous covered surfaces.

As large papillomas are obstructive, exudative, hemorrhagic and liable to infection, they should always be removed, and it would seem to be good practice not to be content to twist the tumor free from its pedicle but, when possible, to excise its base, lest there be unobserved infiltration of the subjacent tissue.

*TUMORS ARISING FROM OR IN CLOSE RELATIONSHIP WITH GLANDULAR
EPITHELIUM*

ADENOMA

An adenoma is a benign tumor whose component elements are arranged like those of an epithelial gland. It consists of a fibro-vascular frame-work in which the epithelial cells are arranged in orderly fashion to form glandular tubules or acini.

Like so many others in pathology, the term adenoma has been abused, through too generous application to lesions and conditions in no way related to one another. But, if the conception of tumor with which we started out be kept in mind, it ought not be difficult to effect the necessary eliminations.

In the first place are glandular enlargements. If an entire gland or a group of associated glands undergoes enlargement, the condition is hypertrophy, not tumor, and ought not be called adenoma. The adenoma sebaceum is such an enlargement, and care was taken to point out that it was not a tumor.

The "enlarged prostate" is frequently spoken of as adenoma, but except in the somewhat rare cases in which it contains circumscribed and encapsulated tumors, there is only hypertrophy and no tumor. Enlargement of its middle lobe, which is circumscribed and independent of the rest of the gland, is still more frequently spoken of as a tumor, but may be but hypertrophy of the prostatic urethral glands. In the literature of diffuse hypertrophy of the mammary glands many cases have been described as adenoma, yet there is no tumor, only hypertrophy. Enlargement of the entire anterior lobe of the hypophysis cerebri is frequently spoken of as tumor, but should be regarded as a hypertrophy.

Next must be excluded malformations of the organs in which portions of their substance—choristas—are separated from the general mass. These are common in the adrenals, and in the thyroid. If these are formed simultaneously with the organ in which they occur, they are more correctly regarded as supernumerary organs, but if they develop later from primordia of residual embryonal cells, they are tumors and adenomas.

Again, it is necessary to eliminate simple hyperplasias, and also, perhaps, some of the complex ones. Hyperplastic endometritis is sometimes said to be adenomatous, but without justification. The gastric polyps, the nasal polyps, and the various soft papillomas have been described as adenomas, because of the presence of glands in their structure, but they certainly are not adenomas, and as has been shown, may not be tumors.

Glandular new formations occurring in the course of regeneration after injury, such as the new formation of bile ducts in certain cases of atrophic cirrhosis of the liver, and recovery from acute yellow atrophy of the liver, are not infrequently said to be adenomatous, and have even been called adenoma, but are in no sense tumors. It makes no difference for the moment whether they be, as is usually believed, new outgrowths from the bile ducts, or atrophic columns of liver cells, they have nothing to do with tumors.

Lastly should be excluded the so-called cystadenomatous formations of the mammary gland described by Schimmelbush. These, we believe, have

no relation to tumors, but are the atrophic mammary acini indicative of ante-
cedent activity, usually of lactation, as will be shown in the section dealing
with the mammary gland.

With these eliminations made, and the definition of tumor in mind, adenoma
is to be conceived of as a benign tumor of glandular structure, beginning at a
focus, developing independently, pushing aside the surrounding tissue as it
grows, and forming for itself a capsule. As such a tumor can only originate from
a primordium capable of glandular development, it naturally makes its appear-
ance in or near glands.

Its structure resembles, in a general way, that of the gland with which it is in
relation, but the resemblance is usually superficial; it rarely perfectly corre-
sponds. It has its own system of acini, and ducts, but the latter do not open
externally or communicate with those of the gland. If they did, we would have
to do with a discrete lobule of the gland, not a separate entity. If it be subject
to physiological stimulation, and secrete, the secretory product accumulates
or is absorbed.

With the exception of the fibro-adenoma of the mammary gland, adenomas
are very rare, but have been observed in almost every gland.

The diverse appearances characterizing the different glands make it impossi-
ble to give an adequate description of the different adenomas; but that is not
necessary. All appear as rounded or nodular, embedded, or rarely peduncu-
lated, encapsulated tumors, the cut surface of which may appear uniform,
fibrillar or fasciculated according to the relative proportions of glandular and
fibrillar tissue of which they are composed.

For the same reason it is impossible to give more than the most superficial
idea of the microscopic structure, but that which characterizes them all is
conformity to the histological structure of the particular gland they imitate.

The greatest interest usually centers about the epithelial elements. In
adenomas following the tubular gland type, these are arranged in tubules; in
racemose glands in acini. But the essential feature is the typical arrangement
of the cells upon a basement membrane, with the retention of their polarity
where the cells of their normal type evince polarity.

Tumors of this kind are always benign. The fact that they are so well
encapsulated and easily removed shows it, yet in almost every case the
question is asked whether the tumor may not be malignant, and the histological
structure is called upon to decide.

The fear that carcinoma of the mammary gland may originate from adenoma
is almost groundless, first because of the extreme rarity of its reported occurrence
and second because when adenomas, or supposed adenomas, do turn out to be
malignant it is nearly always because sarcoma arises in the matrix. The dread
of carcinomatous change has made many pathologists so unduly apprehensive
that the least disorder of the cells in an adenoma is likely to be looked upon as
indicative of beginning carcinoma. As a matter of fact, the epithelium in
mammary adenomas is apt to be more or less disorderly. Instead of being
regularly disposed in a single layer, the cells are frequently excessive, and some-
times piled up so as to completely fill the lumina and even distend them and

sometimes no base line can be demonstrated. Such appearances, however, seem rather to be expressions of an imperfect tumor structure than of malignant change, and too much attention ought not be paid to them. Experience shows that tumors thus characterized do not come back when properly excised.

It is considered good practice to remove the capsule in every case. Blood-good asserts that when this is done, such tumors never return.

Adenomas with the tubular type of structure, and having parenchyma composed of columnar cells, are much less frequent, and occur in the alimentary tract. Quite recently there was brought to the laboratory an almond-sized tumor of the stomach, fairly well circumscribed and partly encapsulated, apparently situated in the muscularis mucosa, and composed almost entirely of tubules resembling those of the gastric mucosa. The arrangement was perfectly orderly, and there was no invasion of the neighboring tissues either by the cells or growing tubules. It was called adenoma, but what might have been its future development is of course unknown. In tumors of this class it is not the orderliness or disorderliness of the epithelium that marks the beginning of malignancy, but the continued growth and extension of the tubules which penetrate the surrounding structures in all directions. It is not until very late, considerable size has been reached, and much adjacent tissue damaged by displacement and compression that the cells begin to scatter in irregular and disorderly groups. On account of this late preservation of order, such tumors have been called *destructive adenomas*.

Columnar or Cylindrical Cell Carcinoma

This is a variety of malignant epithelial tumor arising in, and perhaps from, structures provided with columnar epithelial cells.

Most columnar cell covered mucous membranes are provided with glands of tubular shape, formed by invagination and specialization of the surface covering, or are in relation with the ducts of larger and more specialized type into which the covering extends for some distance, giving them a columnar cell lining.

Whether the tumors arise only from these glands and ducts, or from the surface covering, is an academic question of little interest. It may arise from either or from vestigial embryonal substance.

But however, and from whatever, the tumor arises, one of its most interesting and characteristic peculiarities is its disposition to retain an orderly arrangement of its cells so that it would easily be mistaken for adenoma were it not for its uncircumscribed and infiltrative mode of growth. It therefore does not differ materially from the malignant tumor already described as destructive adenoma or from one later to be considered under the designation *adeno-carcinoma*.

But sooner or later the cells lose their attachment to the basement membrane, separate from one another, undergo more or less anaplasia, and pile up confusedly in the spaces of the tissue. Old lesions of this kind, the centre of which has been destroyed by ulceration may give no indication of their primitive structure and be indistinguishable from *carcinoma globo-cellulare*, the variety derived from cuboidal glandular cells.

It is generally accepted that the tumor originates from the previously well formed and well behaved glands through downward multiplication of their tubules and cells, but this is not certain; what is seen may be only the upward extension of the tumor into the normal tissue which it invades. In well preserved tissues there are usually distinct differences between the normal cells and the carcinoma cells, the latter being larger, with more deeply staining nuclei, and with cytoplasm that is basophilic or polychromatophilic. The arrangement of the cells is also usually less perfect than normal, the glandular spaces or lumina varying greatly; some have scarcely any lumen, others considerable, others may be cystically dilated.

The inevitable result of the growth of the tumor is ulceration of the surface, and disorganization of the tissues below. Secondary infection and inflammation complicate and complete the picture.

Variations in the quality of the tumor result from changes shown by the cells and reaction evinced by the stroma. Some of the tumors grow large and remain soft, the ulceration being slight; others ulcerate early and have their tissue so largely destroyed that they appear more like large shallow ulcerations than like tumors. In some there is great increase in the fibrillar connective tissue of the stroma, so that they become hard and cicatricial in quality.

In some cases the cells evince an abnormal capacity for mucin formation, and the tumor acquires a gelatinous or mucilaginous quality. In a few cases the connective tissue seems, also, to be subject to the mucoid change, and sections show small aggregations of scarcely recognizable frequently vacuolated cells, almost suspended in a gelatinous matrix.

The tumors may long remain local, or may early invade the lymphatics. In either case the secondaries may repeat the original structure; more frequently they repeat the acquired characters. That is to say, they may show beautiful columnar epithelial cells, some of which are still arranged in tubules, although the primary tumor is in an advanced state of mucoid degeneration, or they may show as much mucoid change as the parent tumor.

In the stomach, columnar cell carcinomas may develop from any part of the wall, but are overwhelmingly more frequent in the pyloric third of the lesser curvature where they usually form large fungous masses, soft in consistence, ulcerated upon some part of the surface, and bleeding upon slight traumatism or from vessels opened by the ulcerative and necrotic changes. Eventually these become more and more crateriform until the large mass that may originally have been the size of a man's fist or even a coconut, have disappeared.

In the colon and rectum, ulceration usually takes precedence over fungation and excrescence, and the tumor appears as a deep ulceration, surrounded by massive connective tissue thickening and cicatricial formation. Such are frequently annular and obstructive.

In the body of the uterus, the cavity becomes distended by polypoid masses at the same time that the endometrium and myometrium become invaded. Such polypoid masses may project through the dilated cervix into the vagina, or may necrose and ulcerate, transforming the uterine cavity into an enlarged ragged space with bleeding necrotic surfaces.

Some columnar cell carcinomas if removed early, and before they have infiltrated, do not return, but usually by the time they come under observation, it is too late for more to be hoped for, than postponement of the fatal outcome. If operation be undertaken, it must be radical, and the tumor excised with much of the surrounding tissue. Encouraging results are being reported from the use of X-rays and radium in lieu of surgical eradication.

Carcinoma

Malignant epithelial tumors are collectively and generically known as *carcinomas*. The word, from the Greek, καρκίνος, a crab, seems to have first been introduced into medical terminology by Galen, in the second century A. D., and applied by him to certain indurated malignant ulcerations with peripheral ramifications which he thought bore a fantastic resemblance to the legs and claws of a crab. Later authors, writing in Latin, translated it to "cancer" (crab), in which form it appears in English, while the French modified it to *cancre*, and the Germans retranslated it to "Krebs."

To many writers of the French school, and to a few of the English school of pathologists, cancer is any kind of malignant tumor, so that it is necessary for them to distinguish between epithelial cancer and connective tissue cancer. But in America, where the general trend of German medical thought predominates, it has been the custom to make a fundamental distinction between malignant tumors arising from the connective tissues, which are called sarcomas, and the malignant epithelial tumors which alone constitute cancers or carcinomas.

Carcinoma may be defined as a tumor that results from the lawless and invasive growth of epithelium.

There being three varieties of epithelium, there are three principal varieties of carcinoma: that characterized by squamous cells, that characterized by columnar cells, and that characterized by cuboidal cells.

The first two of these have already been considered, but they are all closely related, as is shown by the following tabulation of the clinical and pathological varieties:

I. Characterized by cells of the squamous type.
   A. Carcinoma planocellulare.
     Squamous epithelioma.
       Composed of cells of the basal layers.
        Carcinoma basocellulare.
         Ulcus rodens.
       Composed of cells of the upper layers.
        Carcinoma spinocellulare.
        Carcinoma parakeratoides.
       Composed of cells similar to those of the hair follicles
        Carcinoma trichocellulare.
         Benign cystic epithelioma.
II. Characterized by cells of the columnar type.
   B. Carcinoma cylindrocellulare.
     Carcinoma tubulosum.
      Malignant adenoma.
      Adeno-carcinoma.
      Carcinoma cysticum.

III. Characterized by cells of the cuboidal type.
  C. Carcinoma rotundocellulare.

Pathological varieties

(a) Carcinoma solidum.

Clinical varieties

1. Carcinoma scirrhosum— Desmoplastic carcinoma.
                    Hard cancer.
                    Withering scirrhus.
2. Carcinoma simplex— Simple cancer.
3. Carcinoma medullare— Carcinoma molle.
                    Soft cancer.
                    Encephaloid cancer.
4. Carcinoma gelatinosum—Carcinoma cylindromatosum.
                    Carcinoma gelatiniforme.
                    Carcinoma muciparum.
                    Mucinoid carcinoma.
                    Mucoid carcinoma.
                    Colloid carcinoma.

(b) Carcinoma tubulosum.
    5. Carcinoma adenomatosum.
        Adeno-carcinoma.
        Carcinoma folliculare.

Non-specific peculiarities, not definite varieties.
  Carcinoma mastitoides.
  Carcinoma psammosum.
  Comedo-carcinoma.
  Osteoplastic carcinoma.

It is at present generally accepted that the cancer cells are the riotous and disorderly descendants of those of the gland in which the tumor develops, and many write and teach as though it were a proven fact; in reality it is but a theory The histogenosis of the carcinoma cells is not known; it is simply believed that they thus originate.

Carcinomas, like other tumors, have focal beginnings from which the growth proceeds in every direction, destroying the antecedent structures and replacing them by its own tissue. A mammary gland, for example, does not "become carcinoma" in the sense of having its normal parenchyma transform into tumor; it does so through the gradual destruction and displacement of its tissue by the multiplying and invading cells of the tumor, which crowd the normal structures out of existence.

Whether the primordium be normal gland, embryonal residual cellular material, or something else, the tumor usually grows from a single center—in rare cases from several centers—by continuous multiplication of its cells which soon lose their polarity, and neglect all boundaries, forcing their way into the tissue spaces and crevises, compressing and destroying the more specialized neighboring parenchyma, penetrating into the neighboring glandular and lymphatic spaces and channels, so as to ramify throughout a great extent of the originally affected organ, and frequently to extend to others.

The result is a continuous dendritic cellular mass that invades the affected tissue like the roots of a plant.

Growth is naturally most easy in directions of little resistance, so the cells first fill the natural passages of the glands —alveoli, ducts, and cystic spaces— and then the lymph spaces and channels, which afford opportunity for almost unlimited extension. Along the lymph-vessels the cells may be transported by currents of fluid to the neighboring nodes, or in case the vessels are obstructed by cell accumulation, in a reversed direction, so as later to grow in unexpected places. Or, they may grow along the lymph-vessels in solid strands or in single file, the older cells dying behind as the younger continue to multiply and advance.
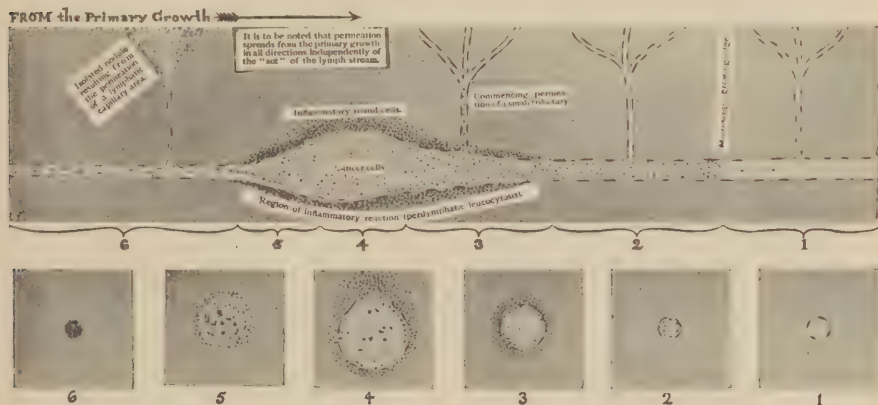
FIG. 247.—Scheme to illustrate the advance of carcinoma permeation along a small lymph-atic, seen in the upper figure in longitudinal section and in the lower figure in a series of trans-verse sections. The lymphatic is finally destroyed by peri-lymphatic fibrosis. 1. Normal lymphatic shortly to be invaded by the advance along it of permeation. 2. Lymphatic permeated by cancer cells, but not yet distended. Note the absence of inflammatory reaction in this region. 3. The lymphatic distended by growing cancer cells. The central cancer cells are becoming degenerate. 4. The lymphatic ruptured by the growing cancer cells: an event followed by vigorous inflammatory reaction. 5. The mass of degenerate cancer cells enclosed in a false capsule of newly-formed fibrous connective tissue. 6. The cancer cells are finally strangled by contraction of the fibrous capsule. The original lymphatic is now represented simply by a thread of fibrous tissue, the cancer cells having been destroyed. (*Handley, Choyce and Beattie, "System of Surgery."*)

No crevice can escape them, and scarcely any structure can resist them. From the original seat of trouble, they extend to neighboring tissues and organs, infil-trating the fascia, the integument, the adipose, the cartilages, the ligaments and the bones. The latter are first penetrated by way of the blood and lymph channels, the cells filling the marrow spaces, and crowding their way between the lamella, until the absorption of the bone itself, is followed by rarefaction and softening that destroys its stability and makes it subject to fracture upon the least effort.

The growing cellular extensions form loose or compact masses with cells irregularly packed together, or occasionally arranged in glandular patterns. They are separated from one another by intervening connective tissue in which the vessels are distributed. It is partly pre-existent, largely newly formed. No intercellular substance separates the cells, and into the cell masses no capillaries ever penetrate. The cells are nourished by intercellular lymph that collects

in the spaces and baths them, and those nearest the nutrient supply fare best and grow while those farthest away degenerate and die. The ability to obtain sufficient nourishment seems to be one of the prime factors in the size of the cell nests. In loose structures with a plentiful lymph supply, they may become very large; in denser tissues with less lymph and more resisting connective tissue they remain small. As the cells multiply they become more and more anaplastic until their resemblance to the cells of the structure in which the tumor grows

FIG. 248.—Carcinoma invading the pectoral muscle in a case of mammary cancer. The muscle fibers in transverse section are clearly shown above, the cancer invading from below.

may be entirely lost. Too rapid multiplication under adverse conditions of nutrition, results in a great variety of cell abnormalities. There may be numerous large cells with immense nuclei, or large cells with several nuclei—physalides. There may be mitotic figures, some perfect, many imperfect and evidently representing miscarriages of cell multiplication.

Some of the healthy cells have the normal number of chrosomes, some the reduced number. There are also cells with inclusions presenting a variety of forms, some of which seem to be other epithelial cells, some leukocytes, some lymphocytes. Some are undoubtedly vacuoles, in which may be dots of protein precipitated by the fixatives, and giving appearances highly suggestive of protozoan parasites, and formerly described as such.

In large cell nests there are usually dead and dying cells in every stage, among which are living and healthy appearing cells, and sometimes both of these are surrounded by quantities of amorphus matter formed by the disintegration of the dead cells.

But together with this activity of the epithelium goes hand in hand a proliferation of the connective tissue by which the cancer stroma is formed. Some of it, as was already said, is antecedent, but most of it is new, and arises through proliferation of the connective tissue in juxtaposition to the cells. Some suppose that it is the effect of irritation from their metabolic products, others that is results from their disintegration products. However that may be, the two grow side by side, and in artificial cultures of cancer *in vitro*, both grow, the connective tissue rather better than the epithelium. The balance between the growth of the epithelium and the connective tissue is the source of the difference between the hard and soft cancers.

The presence of the blood-vessels in the stroma, and their absence from the cell masses, prevents any direct relationship between cells and vessels, and explains why metastasis through the blood, so usual in sarcoma, occurs only rarely in carcinoma.

On the other hand, the infiltrative quality, which is more pronounced in carcinoma than in any other tumor, and the universal disposition to extend into the lymph spaces, joined to the fact that the cells are free—not bound together by intercellular substance of any kind, —explains why metastasis to the lymph nodes is so common and so early.

But blood-vessels are no more exempt from the invasion of the carcinoma cells than other tissues, and if in their way, become penetrated, first by way of the perivascular lymphatics, until the walls are thinned and weakened and prone to yield. The greater number of veins and the thinness of their walls determines that they most frequently suffer.

There may be penetration of the walls and growth of the cancer cells in the interior of the vessel, or disruption of the vessel wall followed by thrombosis, or rupture followed by hemorrhage. Thrombosis predisposes to nutritive disturbance of portions of the tumor; penetration by the cancer cells to metastasis through the veins; disorganization of the vessel wall to hemorrhage.

FIG. 249.—Section of human lung showing many nodules of secondary carcinoma. (*From a specimen in the museum of the Henry Phipps Institute, Philadelphia.*)

rhage. External hemorrhage weakens the patient, or may kill him according to the quantity of blood lost.

Carcinomas occur in both sexes and at all ages, but they are for the most part, tumors of the second half of life. In very rare cases they have been congenital;

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in a few cases have occurred during infancy; and in few cases have occurred during adolescence, but they increase rapidly in frequency after adolescence, and reach the maximum during the third, fourth and fifth decades, during which at least 75% of the cases occur.

During the sixth and seventh decades of life, the number of cases again declines.

The relative frequency of carcinoma in the different organs of the body, and in the two sexes is shown in the following tabulation, based upon the British Mortality Returns for the years between 1897 and 1900, and comprising 102,685 deaths. It is taken from "The Natural History of Cancer" by W. Roger Williams.

Localization	Deaths		Death-rate per million living	
	Males	Females	Males	Females
Mamma, uterus and reproductive organs....	726	25,151	12	384
Stomach................................	8,369	8,355	136	127
Intestine...............................	6,312	6,731	103	103
Liver..................................	5,532	8,654	90	132
Oesophagus.............................	2,358	852	38	13
Tongue................................	2,124	271	35	4
Throat.................................	891	334	15	5
Lip....................................	647	74	11	1
Mouth.................................	508	115	8	2
All parts.............................	40,317	62,368	657	952

The most frequent seats of carcinoma are the mamma and uterus in women. The tumor rarely attains to any considerable size before it reaches a surface and ulcerates (carcinoma apertum). Through the ulceration the tumor is able to grow unopposed, and not infrequently projects as a great fungous mass, soft and cellular in composition, and red and hemorrhagic in quality (fungus hematodes). From the cavity of the uterus such a mass may project for a considerable distance into the vagina. Cancer of the pancreas soon invades the duodenum, where it is then able to ulcerate and invade. Occasional cancers are situated where growth on all sides is possible, and no particular surface reached, as, for example, the ovary, and where no ulceration occurs. Large areas may then soften, but without penetration of the surrounding wall.

Following the ulceration soon comes infection, and from the open lesions there is always more or less lymphorrhagia and hemorrhage, so that the patient eventually falls into a state of depraved nutrition or diminished vitality known as *cachexia*, that sometimes shortly, sometimes long precedes the fatal termination.

Metastasis almost always occurs, first in the regional lymph nodes, later, as these barriers are passed, to the lung, when the cancer is external, to the liver

when it is abdominal. These enlarging in size at the expense of the essential organs may of themselves be the cause of death.

Carcinoma is thus seen to be a highly malignant and fatal tumor. When it is small, and its infiltrative tendency slight, and when no metastases have yet occurred, it may occasionally be successfully eradicated, but unfortunately cases in which this is possible are rare; usually by the time the patient is sufficiently concerned to seek advice, metastasis has already occurred, and little hope of cure to be entertained.

With the most radical operative treatment, under such conditions, little more is to be expected than the postponement of the recurrence, and its occurrence in internal organs where its ravages are less obvious than at the original seat.

For nearly a century surgeons have struggled with the "cancer problem," and in the case of the most frequent form, the mammary cancer, where the superficial position of the organ affected would seem to offer the best opportunity for early discovery and successful extirpation, have devised many operations of increasing thoroughness in the hope of cure. The inventor of each has claimed a maximum of benefit, and a minimum of recurrences, but with the lapse of time, experience has shown that the "path of cancer leads but to the grave." However, surgical removal supplemented by exposure to the X-rays or radium is the best treatment that can be practiced at present.

In order to obtain the maximum of benefit a few important facts should always be taken into consideration. As the distribution of the cancer cells is chiefly through the lymphatics, the tumor should be subjected to as little manipulation before and during the operation as possible. As some manipulation is inevitable, and as there is always the probability that invasion of the lymph nodes has already occurred, the regional nodes should always be removed first, and the cancer or the organ containing it afterwards, at the same operation. As the carcinoma cells are transplantable, care should be taken not to incise the tumor, or if this be unavoidable, to immediately reject the knife thus polluted, for another with which to continue the operation.

As cancer cells are more susceptible than normal cells to the destructive effects of X-rays and radium, the operation should be immediately followed by exposure to their influence in order that any nests of cells beyond the scope of the operation, may meet with their destructive influences, before they have a chance to increase on account of the abnormal conditions induced by the operation itself.

In 1838, Johannes Müller made the first serious attempt to classify cancers, in his book "Ueber die feineren Bau und die Formen der krankhaften Geschwülste." Since that time it has been tried again and again, but with very little improvement. A difficulty that stands in the way of success is uncertainty as to the meaning of some of the most commonly employed terms. For example, "carcinoma simplex" is a term to be found in almost every book upon the subject. But what does it mean? If the rule of nomenclature adopted in most scientific work, that of using every term in the sense in which it was first employed, were followed, a surprising result would be reached. Carcinoma

simplex is by some a term used for the gross morbid description of the tumor itself; by others it is used as descriptive of the histological structure of the tumor.

In either case it usually is descriptive of tumors occupying a position midway between the scirrhus or hard tumors with small nests of epithelial cells on the one hand, and the soft cancer with large nests of cells on the other. This usage seems to have been derived from a table of synonyms appended to the section upon "Epithelial Tumors of the Mammary Gland" in Edward Rindfleisch's "Lehrbuch der pathologischen Gewebslehre zur Einfürung in das Studium der pathologischen Anatomie" (1867). From this it entered into Birsch-Hirshfeld's "Pathologische Anatomie," (1889), was then adopted by Orth in his "Lehrbuch der speziellen pathologischen Anatomie," (1889), and thereafter has been adopted by authors generally. Rindfleisch, in an Italicized parenthesis, attributed the term to Förster, but it does not seem to occur in his writings, and we find that it was used as early as 1838 by Johannes Müller, not in the sense just given, but *as a synonym of scirrhus!* There is really no precedent for the employment of the term in pathological histology.

The meaning of the term "adeno-carcinoma" is equally uncertain, and by whom it was first employed seems not to be known. Tendeloo attributes it to Orth, whom he says divided carcinomas into:

1. Kancroid—cornifying or epidermoid cancer.
2. Glandular cancer—adeno-carcinoma.
3. Cancer—characterized by atypical lawless collections of carcinoma cells.

This grouping leaves one in doubt whether the tumor designated "adeno-carcinoma" arises in the gland or is structurally like it. Tendeloo considers any carcinoma containing gland-like elements as adeno-carcinoma. Ewing defines adeno-carcinoma as "a type in which the growth reproduces more or ess completely, the original gland alveoli from which the tumor springs. It is a partially developed form of carcinoma in which the arrangement of the cells in alveoli with a central lumina, the polarity of the cells, and frequently some trace of their function are partially preserved." Adami makes it synonymous with malignant adenoma. MacCallum says that tumors with a "tendency to form gland-like structures *lined with cylindrical epithelium* are called adeno-carcinoma." He speaks of it only under the description of cylindrical celled carcinomata. Borst thinks that "carcinomas whose structure imitates glands ought to be called *carcinoma adenomatosum*, adeno-carcinoma being reserved for combinations of adenoma and carcinoma."

It is impossible to give an adequate description of the gross morbid appearance of carcinoma unless the organ in which it occurs be taken into account. In general, however, carcinomas are all characterized as embedded, sessile, or pedunculated new growths of irregular outline, associated with tissue invasion, connective tissue induration, and superficial ulceration. Upon section their tissue rarely appears uniform, but is commonly variegated and mottled, and is made up of an alternation of whitish or pinkish fibrillar matricial substance speckled with pink—groups of cancer cells,—and yellow—fat. Variations of color also result from various degenerative changes, and hemorrhagic extravasations.

It is customary at present, to describe four *clinical varieties* of carcinoma, of which three are well characterized, and one doubtful.

1. *Scirrhus.*—This was first described by Galen, as σκίρροσ, and is a hard tumor of small size and slow growth, with limited invasive tendency and late metastasis. Cases have been known to last for as long as twenty years without great damage to the general health.

2. *Carcinoma Simplex.*—This term was used by Johannes Müller as a synonym for the scirrhus just described. It is now employed by many to tumors neither distinctly scirrhus, nor medullary.

3. *Medullary.*—This was first described by Burns, as a soft tumor, some-times of almost brain-like texture—hence sometimes also sometimes called *encephaloid carcinoma.* It forms a large soft tumor—*carcinoma molle*—of rapid growth, and it may be fatal in two or three years.

4. *Gelatinous.*—This term appears in the writings of Otto, Laennec, and Cruveilhier, and applies to an extremely soft tumor, in the tissue of which there are spaces—alveoli (hence in some of these early writings it is occasionally called *alveolar carcinoma*)—filled with more or less clear, colorless or yellowish jelly. It is slow growing, and is one of the least malignant varieties. It was almost universally called *colloid cancer* until a few years ago when the word colloid became restricted to the secretion of the thyroid gland.

The histological study of carcinoma has been pursued with great enthu-siasm for the greater part of a half century, but with great disappointment. It was hoped that it would explain the disease, discover its cause, and make more accurate prognosis possible, but in these most important particulars it has largely failed. Many interesting facts have been discovered, but none of prime importance. It has, however, added a microscopic variety to the clincial varieties previously known, the adeno-carcinoma.

The histological structure of any carcinoma usually lacks uniformity; one part may appear like scirrhus, another like medullary, while the greater part fails to corre-spond with either, and perhaps on that account has come to be so often called carcinoma simplex for want of a better term.

The different appearances of the different parts probably depend upon different ages and conditions, and the quality of the tissue in which the tumor is growing. No diagnosis should be made from the ex-

FIG. 250.—Scirrhus carcinoma in the mammary gland. Section through an amputated organ. *a*, Tumor; *b*, adipose tissue; *c*, pectoral muscles; *d*, metastatic nodule in the muscle. (*Johres.*)

amination of a single section from a single part of a tumor.

1. *Carcinoma Scirrhosum.*—Sections of this tumor show a dense fibrillar connective tissue matrix in which the essential cells are distributed without
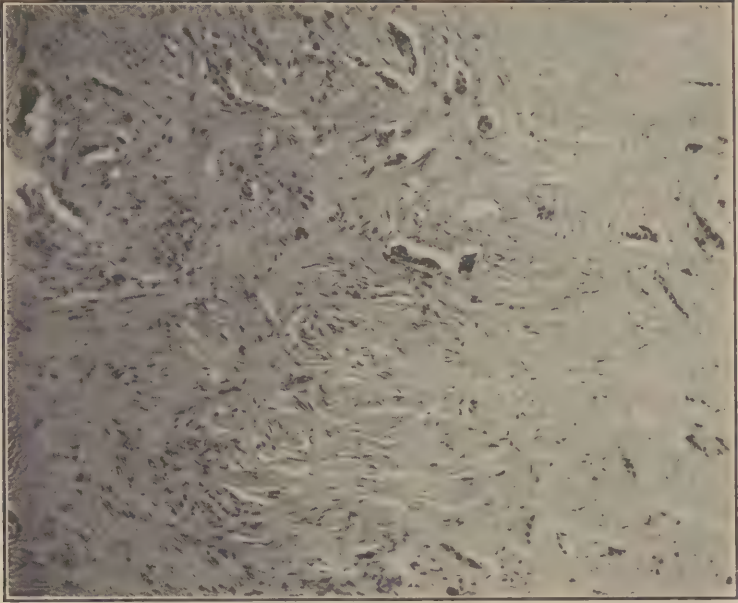
Fig. 251.—Microscopic section of a scirrhus carcinoma of the breast.

Fig. 252.—Section through an entire mammary gland containing a small encephaloid or medullary carcinoma. (*From a case operated upon in the Lankenau Hospital of Philadelphia.*)

arrangement, in relatively small groups. The spaces are solidly filled with cells, hence this tumor, like the following, is sometimes further designated *Carcinoma solidum*. The tumor is hard because of the preponderance of the fibrillar tissue over the epithelial elements. Rarely the epithelial cells are found partly in a state of fatty degeneration, which is supposed to be the result of the contracting and compressing effect of the connective tissue stroma. It is, indeed, stated that, in rare instances, this may reach such a degree as to effect destruction of all the cells and a natural recovery from the tumor. Tumors of the breast of
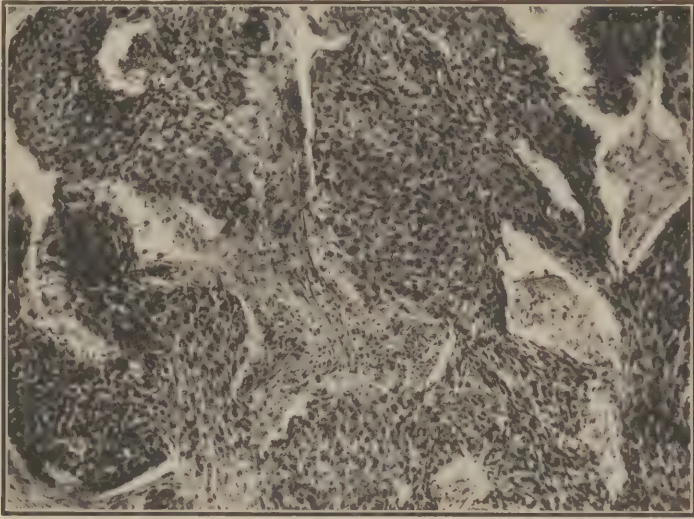
FIG. 253.—Microscopic section of an encephaloid or medullary carcinoma of the breast.

slow growth, great chronicity and pronounced contraction are sometimes described as "withering scirrhus." The stroma of these tumors sometimes calcifies.

2. *Carcinoma Medullare.*—The greater part of this tumor is made up of such large and closely approximated cell nests as to give the appearance of an almost purely cellular structure, and bear a close resemblance to sarcoma. The tumor grows rapidly because it is so largely composed of cells. But the rapidity of growth and cellular character may have something to do with the quality of the tissue in which the tumor grows, as scirrhus tumors seem to be more frequent in slender women with small mammae, and medullary tumors in stout women with large adipose breasts.

When the medullary carcinoma ulcerates, fungation with the formation of large projecting tumor masses soon occurs. Covered with necrotic cells which afford a nidus for saprophytic micro-organisms, this soon becomes extremely offensive.

3. *Carcinoma Simplex.*—This is by far the most frequent variety. It is neither scirrhus nor medullary; that is, it is not so uniformly composed of small cell nests as the scirrhus, nor so uniformly of large ones as the medullary. It is

a non-de-script or intermediate variety—at least, such seems to be the usage of the term adopted by the majority of authors of the present time. Different portions of these tumors may show different pictures. Certain areas may resemble scirrhus, others medullary carcinoma.

4. *Carcinoma Gelatiniforme.*—This tumor, formerly called colloid cancer, occurs in two forms.
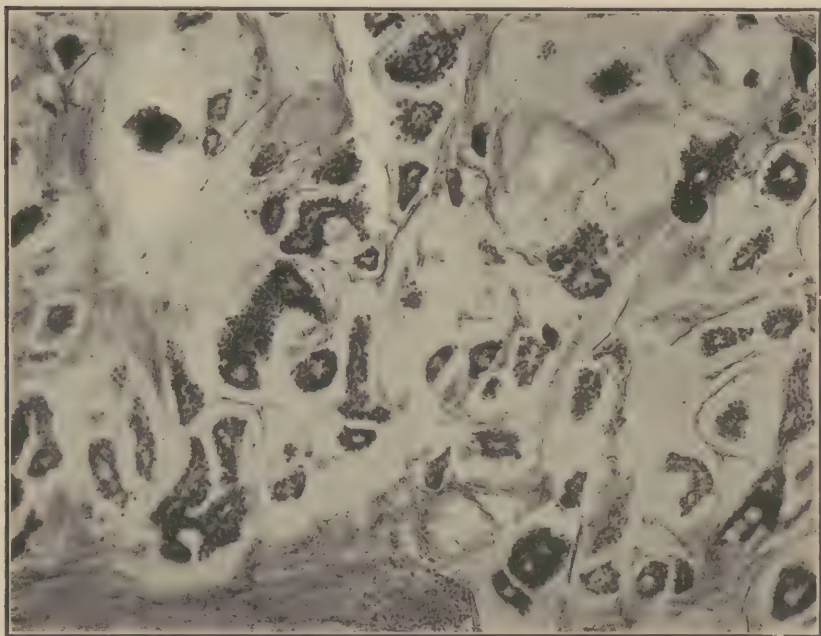
FIG. 254.—Microscopic section of a gelatinous carcinoma of the breast.

A. Gelatinous Carcinoma of the Mammary Gland.—In this variety, the nests of cancer cells are usually small, and frequently fairly well-preserved, though each is surrounded by a considerable accumulation of colorless jelly-like material——mucoid (?)—forming a considerable space or alveolus in the stroma—*alveolar carcinoma.* The source of the jelly is not clear. As the spaces are large and the cell nests small, it may be formed through mucinoid degeneration of the outer cells. But as the outer cells are nearest to the sources of nutrition and oxygen, it seems strange that they should be the first to suffer. On the other hand, as most of the stroma of the tumor is softened, and gelatinous, it may be that the mucous is derived from it and is connective tissue mucus. In many cases it seems as though the mucus was derived from both sources.

B. Gelatinous Carcinoma of the Alimentary Tract.—This usually occurs either in the stomach or in the rectum. In the former the pyloris is the most frequent seat. The gross appearances vary considerably, some being large soft tumors, others of relatively small size, characterized by the presence of what appear as vesicles or cysts filled with clear jelly, usually of amber color. These not only

occur in the substance of the tumor, but upon its surface, and in and upon the neighboring and invaded lymph nodes.

The histological examination shows that the tumor may be either carcinoma cylindrocellulare, or carcinoma rotundocellulare. In either case the differentiation may be difficult to make because of the high degree of morbid change evinced by most of the cells. The general appearances are comparable to those of the preceding variety.

In the rectum the tumor is always carcinoma cylindrocellulare, and in areas not too far gone in the mucinoid degeneration, the appearance of the cells is interesting and instructive. Ordinarily, when columnar epithelial cells form mucin, it appears in the form of a vacuole in the distal two-thirds of their substance, from which it is discharged upon the surface, and there swells to form the structureless mucus. But in carcinoma, the cells no longer maintain their relation to the surface, but are in the depths of the tissue; they also no longer retain their polarity, and as anaplasia more and more disturbs their morphology, they assume more and more nearly the spherical form. Under these circumstances any mucin formed in their substance is more centrally situated, and the cells become large spheres in which the increasing droplet of mucin swells more and more until it gives each cell the form of the "seal ring." As the cells eventually rupture and liberate their contents, the mucin absorbs water and swells to form mucus, which distributes among the cells, widely separating them. Except in well preserved portions of such a tumor, in which the cell degeneration is moderate, it may be difficult, and sometimes impossible for a beginner to make the diagnosis.

The proof that the gelatinous carcinoma is a distinct and separate variety, and not a mere degeneration of the more frequent forms, seems to be found in the regularity with which the gelatinous structure is repeated in the secondary tumors.

5. *Carcinoma Adenomatosum: Adeno-carcinoma.*—As nearly as can be gathered from a careful survey of the literature, this is a tumor the greater part of which, regularly imitates the structure of a gland. The proof that this is an essential quality is found the repetition of the alveolar structure in its metastatic secondaries. It occurs most frequently in tumors arising in connection with columnar epithelium, but may also occur in those having cuboidal cells.

There seems to be no justification for calling any carcinoma arising in a gland an adeno-carcinoma. Care should be taken not to mistake the antecedent glandular tissue in which the tumor grows for part of the tumor.

Occasional carcinomas having large cell nests show extensive necrotic change of the central cells with perfect preservation of the outer ones, an appearance suggesting dilated ducts filled with amorphus granular material— *comedo-carcinoma.* Unless it can be shown that such tumors show the more usual type of gland imitation, they should not be classed among the adenocarcinomas.

The actual gland resemblance in adeno-carcinoma may be slight, and does not necessarily correspond with that of the particular gland in which the tumor grows. Thus, if in the mammary gland, it is not necessary that the tumor

repeat the structure or arrangement characteristic of that organ.   Should such an arrangement be found, it would suggest that pre-existing breast tissue was being mistaken for the tumor.   Side by side with non-de-script gland-like units, irregular carcinoma units occur.

All varieties of carcinoma are subject to modifications of histological appearance brought about by internal and external accidents.   The former have to do
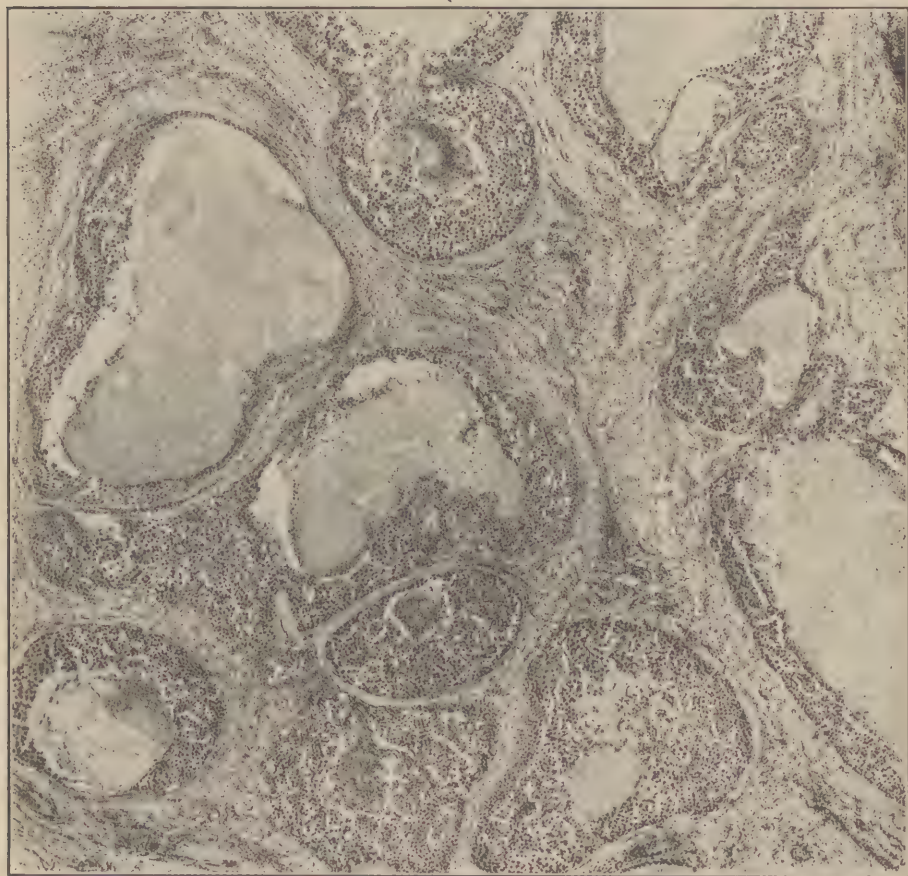
FIG. 255.—Microscopic section of a comedo-carcinoma of the breast.   (*Binney*.)

with the adequacy or inadequacy of the blood vessels, and their invasion or exemption from invasion by the tumor cells, with resulting alterations of good and bad nutritive conditions, localized interstitial hemorrhages, cell degenerations, necrosis, ulceration etc.; the latter, with infection.   To seize upon these modifications as criteria for the establishment of new varieties seems to be without practical advantage, and to introduce new terms by which to describe them, a useless burden upon nomenclature.

CYSTS

A cyst is a well circumscribed, pathological collection of fluid, tending to persist and increase.

The term is used with considerable latitude, and different authors seem to have different ideas as to what is fundamental. For example, when seventeen different definitions from as many different sources were analyzed, it was found that five regarded the *sac* surrounding the fluid as the cyst; nine, the *space* occupied by the fluid as the cyst; and three regarded the collection of *fluid* itself as the cyst.

The fluid may collect in an antecedent space with a well defined wall, lined with epithelium, as when retained in the duct of a gland; or may create space for itself at the expense of the antecedent structures, as in cysts of the brain, and the wall by which it is separated from the surrounding tissue develop only after it has existed for some time.

The fluid may be a normal product of the body, or an entirely abnormal one, or it may have been a normal one that becomes abnormal through dilution, inspissation, precipitation or pathological addition. On this account many of the definitions expressly state that a cyst contains "fluid, semi-fluid or solid" contents.

That some kind of a sac or wall must surround and retain the fluid goes without saying, but it need not be primary, is not indispensible, and may be present only as an end result.

Thus, an area of softening in the brain, a hemorrhage into the brain, or an abscess of the brain, may result in the formation of a space filled with fluid—a cyst—though for a long time it has no other confines than surrounding softened nervous tissue; some time later endothelium from the perivascular lymphatics may line it, still later the cellular lining may be reinforced by connective tissue derived from the perivascular sheaths, and a definite wall formed. Was it not just as much a cyst before the wall developed as afterward? Marchand would say no. He regards only those with distinct walls as *true cysts;* others are *false cysts*.

The duct of any gland, may be obstructed and the secretion held back. It then dilates and a cyst is formed without any other wall or sac than the tissue of the duct. In such case is it not the collection of fluid, rather than its inclosing envelope that is the formation of the cyst? Should such a cyst persist, and increase, its delicate epithelial membranous wall becomes reinforced in consequence of the survival and condensation of the connective tissue of the gland, whose parenchyma disappears from pressure atrophy.

Ribbert is emphatic upon the principle that every cyst depends upon the growth of its sac as well as upon the accumulation of its contents. He supposes that if the sac did not grow, it must distend to its limit, and burst, which he says it never does. That is by no means certain, though difficult to determine.

There are not infrequently seen upon the surface of the kidney "retention cysts," with extremely thin walls that seem as though they would burst upon the slightest pressure, but being internal, and filled with harmless contents, their rupture might never be recognized. Cystic kidneys sometimes show superficial

scars appearing to result from the rupture of cysts. Branchial cysts and median cervical cysts frequently rupture, and thus give origin to fistulas. It seems to be pretty generally recognized that as superficial cysts become larger their walls tend to become thinner, so that the growth, of the cyst wall though it may occur in some or even all cases does not seem to be quite so important as Ribbert would lead one to think.

Cysts are never thought of as having outlets, but occasionally they may. The formation of retention cysts usually depends upon the complete closure of the duct of the gland, but it may remain partly open. All that is necessary is that the secretion form more rapidly than it can escape, when some of it must be retained, and a cyst may be formed. Sheild, in his book upon "Diseases of the Breast," figures a specimen preserved in the Museum of the St. George's Hospital, in which "a bristle is passing through one of the main ducts, straight into a cyst of the mamma."

It is sometimes stated that the contents of the cyst are secreted by cells of its wall. That is misleading, and not always true. An examination usually quickly convinces one that the cells are in no condition to secrete, and in large cysts there may be no epithelial cells to do so. The contents are furnished by slightly changed glandular elements that communicate with the cyst, and pour their contents into it, but are not a part of it.

Some of the definitions assert that the contents are "morbid." This may be, but is not necessarily true. A recent cyst in the lactating mammary gland contains milk; one in the salivary gland, saliva; one in the kidney, urine; one in the liver, bile, and so on. It is true, however, that as time goes on, all of these secretions may become so modified as not to be recognizable, but originally they were not "morbid."

It is almost as difficult to give a satisfactory discussion of cysts as it is of tumors; there are too many varieties and too many exceptions.

The following tabulation seems to afford a convenient approach to the subject:

I. True cysts.
   1. Originating in pre-formed spaces.
     A. Originating in embryonal vestigial structures—congenital.
       (a) Lined with squamous epithelium.
         Sequestration dermoids—from ectodermal inclusion.
         Allantoic—urachal—cysts.
       (b) Lined with columnar epithelium, which may be ciliated.
         Thyro-glossal cysts.
           Congenital cysts of the epiglottis.
            Subhyoidian ranulas.
         Omphalo-mesenteric cysts.
           Umbilical.
          Intestinal.
         Wolffian cysts.
           1. In the male.
            Cysts of the upper paradidymis—organ of Giraldes.
            Cysts of the lower paradidymis.
            Cysts of the vasa aberrantia of Haller—spermatoceles.
            Retro-vesical cysts.

Retro-peritoneal, omental, mesenteric cysts.
2. In the female.
Cysts of the paroöpharon—parovarian or intra-ligamentous cysts, from Kobelt's tubes.
Cysts of Gärtner's Ducts.
Retro-peritoneal, omental and mesenteric cysts.
Müllerian cysts.
Cysts of the stalked hydatid or appendix epididymis.
Cysts of the sessile hydatid.
Pronephric cysts.
Cysts of the hydatid of Morgagni—morgagnian cysts.
Mesonephric cysts.
Retro-peritoneal cysts, omental and mesenteric cysts.
Metanephric cysts.
Congenital cystic kidney.
Neurenteric cysts.
Ano-sacral cysts.
(c) Lined with either squamous or columnar epithelium or both.
Branchial cysts.
(d) Lined with endothelium.
Cysts of the round ligament of the liver.
Hygroma colli cysticum.
B. Arising from mature structures.
The cyst is originally lined with epithelium.
(a) The cyst arises through obstruction of normal outlets—retention cysts.
1. The cyst develops in a gland.
Bartholin's glands.
Cervical glands of the uterus—Nabothian follicles.
Cowper's glands—Cowperian cyst.
Epididymis—spermatocele.
Gastric and intestinal glands.
Kidney—retention cysts.
Lacrymal gland—dacryocyst.
Liver—biliary cyst.
Mamma—galactocele.
Meibomian glands—Chalazion or tarsal cyst.
Pancreas—pancreatic cyst.
Prostate—prostate cyst.
Salivary—submaxillary—ranula.
Sublingual—ranula.
Blandin Nuhn—ranula.
Parotid—Stenson's cyst, cyst of the cheek.
Labial.
Lingual.
Epiglottic.
Sebaceous—comedo—wen.
Sudoriparous—milium.
Urethral.
2. The cyst develops in a hollow organ.
The appendix vermiformis—mucocele.
The gall bladder—hydrops vesicae felleae.
The uterus—hydrometra.
3. The cyst develops in a conducting tube.
The Fallopian tube—hydrosalpinx.
The ureter—hydro-ureter—hydro-nephrosis.

     (*b*) The cyst arises through accumulation of secretion in closed spaces.
          In the corpus luteum.
          In a Graffian follicle.
          In the pituitary.
          In the thyroid—colloid and cystic goitre.
          In a tooth follicle—dentigerous cyst.
    The space was originally lined with ependyma.
      Neural cysts.
        Encephalocele.
        Hydrocephalus internus.
        Hydromyelia—Syringomyelia(?).
        Spina bifida.
    The space was originally lined with endothelium.
      Arachnoid cysts.
      Bursal cysts.
        Hyoidian—Boyer's cyst.
        Metatarso-phalangeal—bunion.
        Olecranar—miner's elbow.
        Patellar—housemaid's knee.
        Ischiatic—weaver's bottom.
        Chylous or lacteal cysts of the mesentery.
        Hydrocele.
        Hydropericardium.
    Formed through hernial protrusion through the walls of antecedent serous
      spaces.
      Ganglion.
      Synovial cysts—Baker's cysts.
      Crab's eye cysts formed over Heberden's modosities on the fingers in arth-
      ritis deformans.
  2. Originating in newly formed spaces, following traumatism with dislocation of the
    surface epithelium.
    Traumatic epidermal implantation cysts.
  II. Neoplastic cysts.
    1. Arising through segmentation and differentiation of sequestered blastomeres.
    Teratoid cysts.
    2. Arising through parthenogenetic development of germinal cells.
    Ovarian dermoids.
    3. Arising through excessive activity of persisting formative tissues.
    Ovarian cystoma—from Pflüger's tubes.
  III. Pseudo-cysts.
    1. Arising through the dilatation of spaces about foreign bodies.
    Adventitious cysts—as a cyst of the iris caused by the accidental implantation of
    an eye-lash.
    2. Arising through tissue disorganization and necrosis.
    Cysts following hemorrhagic extravasation into soft tissues—hematoma.
      Cephalohematoma.
      Hematoma auris.
    Cysts following suppuration in the brain.
    Cysts following necrosis and colliquation in tumors, both of the soft parts and the
    bones.
    3. Arising through fermentation in the tissues;—Gas cysts.
  IV. Parasitic cysts.
    Echinococcus or hydatid cysts.
    Cysticercus.
    Cysts formed about Trichinella spiralis.

It may occur to the reader that the tabulation includes a number of lesions or conditions such as the neural cyst group, encephalocele, hydrocephalus, spina bifida, and the cysts arising through the dilatation of the endothelial lined spaces, especially the hydropericardium and hydrocele, that it would not occur to him to include among the cysts. There is certainly doubt of the propriety of classifying some of these conditions as cysts, but they are introduced not so much because it is believed that they belong where they are placed, as to call attention to the difficulty of determining exactly what a cyst is. It is universally admitted that a bunion is a cyst; if so, the house-maid's knee is also; if so, a hydrocele may be so considered; and then why not hydropericardium? If we include it, why not hydrothorax? What shall be done in the case of ascites?

When a tumor contains an area of softening, the center of which is almost fluid, becomming firmer as the periphery is approached, it is considered by some to be a cyst, but others declare that it is not one until the process of softening is completed, and the softened contents are separated from the surrounding healthy tissue by a distinct membrane. That is the teaching of those that regard the sac as the cyst; but those that look upon the fluid accumulation as the cyst, consider that the cyst is formed as soon as the necrotic tissue is soft enough to be scooped out in the center. If colliquation of tissue and the formation of a space filled with fluid constitutes a cyst, why is not an abscess a cyst? In reality there seems to be no essential difference; an abscess is an inflammatory cyst, though the name is rarely applied to it, and it may be better not so to call it. Some declare that the difference between an abscess and a cyst is that the former results from inflammation, and the latter not. That is an error; nearly all cysts have their beginnings in some form of inflammatory disturbance.

One author introduces into his definition of cyst, the statement that the collection of fluid tends to be of spherical shape. It seems as though that is unnecessary, as it is inevitable. A collection of fluid must exert the same general pressure in all directions, and thus tend to sphericity. If special resistance is encountered in any direction, the shape must be modified accordingly.

It is commonly remarked that cysts are usually upon the surface of the organs in which they occur. This again is inevitable. A cyst in the center of any organ may at first grow against uniform resistance in all directions, but as it increases in size, the time must come when the resistance will be less in one direction than in others, when the growth will immediately become more rapid in that than in other directions, and the cyst will eventually project superficially at that point.

Most cysts are single spaces—*simple* or *unilocular*—but sometimes they are *compound* or *multilocular* that is, composed of several similar approximated spaces. In some cases hairs grow from the inner walls of cysts, as in the dermoids, *piliferous cysts*.

In some cases, as the echinococcus, cysts form within cysts, *proligerous cysts*.

The dimple over the coccyx from which hairs sometimes project, and at the bottom of which there is a little cavity, is sometimes described as *pilocystic*.

Of all those mentioned, that which is most questionable is the *gas cyst*. All definitions of cysts assert that they must contain fluid, semi-fluid, or solid contents. In no case is it stated that they may contain gas.

Cysts vary greatly in size. Those of the sweat glands, meibomian glands, sebaceous glands (comedo), gastric and intestinal mucous glands, are of little more than pin-head size. Those of the lacrymal gland, (dacryocyst) cervical glands of the uterus (Nabothian follicles), and urethral glands, are most commonly of about pea size. The biliary cysts, the retention cysts of the kidney, the ranulas, and cysts of Bartholin's glands, may be as large as a walnut, sometimes as large as a hen's egg. Galactoceles may be as large as a cocoanut;

FIG. 256.—Large ovarian cyst in a Chinese woman. (*Reifsynder*.)

pancreatic cysts as large as a human head. But the largest of all the cysts are those that occur in the ovary, some of which may contain gallons of fluid, and weigh as much as 200 pounds.

With the exception of the ovarian cysts in the group described as arising through the excessive activity of formative tissues, all cysts are benign and do not recur when removed.

The treatment of a cyst should be radical. It is rarely of advantage to incise a cyst; in most cases it simply transforms it into a fistula. The most successful treatment is complete removal of the entire sac by dissection. There are, however a few exceptions; when the formation of the cyst is due to the obstruction of a duct, the removal of the obstruction is sometimes followed by spontaneous diminution and eventual disappearance of the cyst.

In removing any cyst by dissection, it is best not to rupture it, as the collapse of the sac makes the dissection more difficult, except the cyst be very large and have a thick wall.

PART III

SPECIAL PATHOLOGY

SPECIAL PATHOLOGY

THE THYROID GLAND

The normal thyroid gland varies somewhat in size in different individuals, and in the same individual at different times according to the sexual activities, —at least this seems to be the case as the gland swells somewhat at puberty, at in menstrual periods, and during pregnancy in females, and during adolescence in males.

The gland consists of a central portion, the isthmus, and two lateral lobes. Of these the isthmus is probably subject to the greatest variation in size, and may be wanting. According to Piersol's Anatomy, the average measurements are: isthmus, 5mm. to 2 cm. in breadth; lateral lobes, 3 cm. to 6 cm. in height; transverse diameter of the entire organ, 6 to 7 cm., weight, 30 to 40 grammes. In goitre districts a weight of 60 grammes may be considered normal.

Situated at the root of the neck, at the junction of the larynx and trachea, and almost entirely covered by the sterno-thyroid, sterno-hyoid, and omo-hyoid muscles, the gland is usually invisible, and difficultly palpable. If in any case it can be distinctly seen or easily felt, it may be assumed to be enlarged. Moderate enlargement, permitting visibility without actual prominence, is, however, quite compatible with normal physiological variation and must not be considered as goitre or looked upon as indicative of disease.

The histological structure of the thyroid gland is simple, but the description given in some textbooks, is not correct. For example, it is stated in one of the most recent books, "that the gland is made up of follicles, alveoli or acini, each of which is closed and independent of any other, and not connected with any duct." So far the description is correct, but the writer goes on to say that "the normal gland can be recognized by the uniformity in the size of the alveoli, whose only variation is caused by the fact that being more or less mutually compressed, some portions of the alveoli are larger than others, and in the sections, the knife not always passing through the broadest part of the alveolus, some appear larger than others." This is incorrect as shall soon be shown. "The follicles or acini are lined with a single layer of cuboidal epithelial cells, arranged upon a very delicate basement membrane, and are filled with a translucent homogeneous mucilaginous material known as colloid, which is the secretion of the gland, the quantity being quite uniform in the alveoli." In the supposedly normal thyroids that we have examined, the alveoli were not of the same size, or even of nearly the same size. Many of them were fairly large, and fairly uniform, and did contain nearly the same quantity of colloid, but in addition to them, and especially near the superficial portions of the gland were many other alveoli of very small size, some of which contained very little colloid and the smallest of which

contained none at all. There were also occasional collections of cells, undoubtedly of the same character not definitely arranged into alveoli at all. These may be regarded as undeveloped or embryonal elements and may be conceived to be of importance in connection with the enlargements to which the gland is subject.

The colloid seems to arise in two ways; certain of the cells are known as *chief cells* and secrete colloid as minute droplets that are delivered one by one into the general mass, others are known as *colloid cells* and actually become transformed into colloid substance.

The thyroid substance is a viscid jelly, of somewhat variable consistency and complex composition, whose chief purpose seems to be that of acting as a kind of vehicle or excipient for the combination of iodine.

The presence of this element in the thyroid was first pointed out by Baumann who, in 1895, when working in the laboratory at Freiburg extracted an iodid-containing compound to which he gave the name thyroidin, or iodothyrein, which gave no biuret reaction, and contained 14.5% of iodin. Not much advance in the study of the subject was made until 1916 when Kendall took it up and by improved methods succeeded in extracting a crystalline substance containing 65% of iodin, to which he gave the name *thyroxin*.

As no other important physiologically active substances have been found and as these iodin combinations, and especially the thyroxin of Kendall seem able to meet all the requirements of physiological investigation, it is conceded that the iodin is the important component of the thyroid secretion.

GOITRE

Goitre may be defined as *any non-inflammatory, diffuse or nodular, hyperplastic or degenerative enlargement of the thyroid gland, of benign nature.*

Goitres are of sporadic occurrence almost everywhere, but in certain geographical areas, they are endemic, and occasionally become epidemic. Since the time of Hippocrates, who knew many of the clinical facts about goitre almost as well as we, the endemic and epidemic occurrence of the disease has been believed to depend upon some peculiarity of the drinking water.

The observations and experiments of Klinger in Switzerland and Marine and Kimball in this country indicate that there is only one important cause of thyroid enlargement, and that is lack of iodin.   In the case of sporadic goitres the trouble may be assumed to rest with the individual; but in endemic and especially in epidemic goitre it is outside and probably has to do with telluric or diatetic conditions over which the individual has little if any control, but which in some manner diminish his iodin content.

Marine and Lenhart, in 1909 and 1910 made interesting observations upon the brook trout in a large private hatchery in Pennsylvania.   About 2% of the young fishes were affected with enlargements of the thyroid gland, at first regarded as carcinoma, but later determined to be only severe epidemic goitre brought about by overcrowding, overfeeding, and lack of iodin.   When the amount of food and the supply of water were properly adjusted to the number

of fishes in the tanks, and an iodin containing substance was added to the water passing through them it completely disappeared. The amount of iodin needed, as an addition to the water to arrest the thyroid enlargement did not exceed 1: 1,000,000.

The application of the knowledge thus obtained to the prevention of endemic goitre of human beings was first undertaken by Marine and Kimball at Akron, Ohio, in 1917. Their report states:

"The result of our two and a half year's observations on school girls in Akron are as follows: Of 2190 pupils taking 2 gr. of sodium iodid twice yearly, only five have developed enlargement of the thyroid: while of 2305 pupils not taking the prophylactic, 495 thyroids have developed thyroid enlargement. Of 1182 pupils with thyroid enlargement at the first examination who took the prophylactic, 773 thyroids have decreased in size: while of 1048 pupils with thyroid enlargement at the first examination who did not take the prophylactic, 145 thyroids have decreased in size."

"Klinger has recently, (1921) reported even more striking results in the school-children of the Zurich district. He worked with school populations in which the incidence of goitre varied from 82 to 95 % while our maximum incidence in Akron was 56 %. With such a high natural incidence of goitre, his observations necessarily deal more with the curative effects. Thus, of 760 school children, 90 % were goitrous at the first examination. After 15 months treatment with from 10 to 15 mg. of iodin weekly, only 28.3 % were goitrous, of a total of 643 children examined.

"The foregoing results were obtained in adolescents. There are two other periods in life when simple goitre frequently develops, namely, (1) in foetal life, and (2), during pregnancy. While the thyroid enlargements developing about the age of puberty are more common, they are not more important than those developing during pregnancy and foetal life. The higher birth mortality of infants with congenital goitre is well known. The thyroid enlargement of both mother and foetus may be prevented by giving 2 gr. of sodium iodid, or its equivalent in iodin in any other form, during the first half of pregnancy."

Marine and Kimball draw a sharp line of distinction between *simple goitre*, which is common to both man and the lower animals, and includes all those enlargements of the thyroid gland that are commonly known as endemic, epidemic, sporadic and physiological, and *exophthalmic goitre*, which is not known to occur except in man, and is probably a different morbid process.

Only the simple goitres are preventable and amenable through iodin therapy.

The administration of iodin to a patient suffering from an old and large goitre is usually without benefit as the changes are too well established to undergo much, if any retrogression; the usefulness of the agent is probably limited to moderate and early enlargements of the thyroid gland.

The mild goitrous enlargements occurring during adolescence, and chiefly comprising the lesions considered by Marine and his associate, have long been known to be subject to frequent spontaneous diminution on size, and hence were included among the so-called physiological goitres.

It is possible that most goitres are originally compensatory enlargements that become permanent and pathological through inability to successfully compensate, i.e., fix enough iodin to supply the individual requirement.

Through what internal change the enlargement of the thyroid gland takes place is a matter of interest. Virchow attributed it to the new formation of acini by budding from the well-formed adult structures; Wölfler to the development of the embryonal elements with which the thyroid tissue usually abounds,

and to which we have already called attention.   If the groups of embryonal cells be able to multiply indefinitely and form acini, there seems to be no limit to the size to which the thyroid may attain, and indeed this may be very great. Alibert has described goitres that hung down upon the breast, and one that reached to the thighs of the patient.

FIG. 257.—Large cystic goiter measuring 31 inches in circumference, including neck.   (*C. H. Mayo.*)

The goitrous enlargement may be diffuse, and uniform or circumscribed and nodular.   In some cases the entire substance of the enlarged gland is uniform and appears normal except for its size; in other cases there may be a single node, numerous nodules, or the entire gland may appear to be composed of a conglomerate mass of nodules, by which any remaining unaltered original thyroid substance is pushed aside and compressed.

Remembering the distribution of the embryonal tissue through the gland, it is as easy to account for the formation of the nodular as for the diffuse enlargements.   The former represent localized, the latter diffuse developments of these elementary structures.   When such nodules of embryonal thyroid tissue make their appearance in the midst of the adult thyroid structure, the difference in histological appearance is somewhat striking, and has led to the classification of the new growths among the tumors, and as *adenomas* of the gland.

The occurrence of diffuse and nodular enlargements has been for years a basis of classification, and is morbid anatomically valid. It does not, however, bespeak any essential difference in either the nature or origin of the process of enlargement. In the goitres of the school girls studied by Marine and Kimball, there were both diffuse and nodular enlargements, and both depended upon the same cause.

The substance secreted in the adenomas corresponds to that in the thyroid itself, for A. Graham found that either will increase the rapidity of the development of tadpoles into frogs. When present in excess it causes hyperthyroidism, and about 20 % of cases of clinical exophthalmic goitre are found to have adenomas in the thyroid gland.

Differences in the microscopic appearance of these adenomas may best be interpreted as indicative of different stages of the development of the thyroid tissue presumably under the stimulation of the physiological necessity for iodin. Stimulation of a certain kind and intensity may excite the rapid development of new alveoli, which push the preformed tissue aside, crowd and compress it until it becomes surrounded by a capsule of connective tissue. Stimulation of a different quality or intensity may cause the development of a certain number of new alveoli, and then, having reached the size required, proceed to accumulate the essential secretion, in normal amount or in excess.

It must not be supposed, however, that there is no participation of the adult fully formed thyroid tissue in goitrous development, an impression that may have unintentionally been given in attempting to show the importance of the part played by the embryonal tissue. When considerable embryonal tissue is present it attracts attention, chiefly through its nodular formations. When there is little or none, and when it does not develop locally, attention is attracted to the changes shown by the fully developed thyroid tissue, which under these circumstances must bear the whole burden of the enlargement. According to Marine and Kimball this always begins with a decrease in the colloid, and a hyperplasia of the epithelial cells, which normally cuboidal, become columnar, and through increase in number lead to infoldings and plications of the alveolar linings.

Simple goitres, may be regarded as hypertrophic enlargements of compensatory character, intended to facilitate the collection and mobilization of iodin compounds. They are occasionally and incidentally neoplasmic.

When neglected they may become large and permanent, and then may fall into the hands of the surgeon, who may be compelled to remove them, or part of them, either for cosmetic reasons, or because of the pressure they exert upon the other structures of the neck.

But certain physiological facts should be kept in mind.

If a pregnant mammal be deprived of iodin by artificially selecting the food and water with that end in view, the young will be born with enlarged thyroids. In endemic goiter districts, where many of the women are already goitrous, congenital goitre is common, and children born with normal sized thyroids, commonly suffer from enlargement at puberty or later. If these cases be neglected, a number of them may develop good sized goitres, no longer affected

by the administration of the iodin. With or without goitres, some of the children in the endemic goitre districts suffer from cretinism. In these cases the thyroid enlargement is but proof that iodin is needed, the development of cretinism that thyroid secretion is defective. To remove such goitres can neither supply iodin nor thyroid secretion.

On the other hand, the administration of iodin may inhibit the growth of the goitre, and the administration of thyroid substance, or thyroxin, may prevent or cure the cretinism.

A goitre, however, does not necessarily bespeak present need of iodin; it may be but the surviving indication of iodin necessity long past. When it can be shown that such is the case, the surgical removal of a part of the goitre may be undertaken to improve the patient's appearance, or prevent pressure.

But though these facts may seem to make the general subject of simple goitre fairly intelligible, a disturbing ignorance surrounds that other and differently occurring form, the *exophthalmic goitre*. Fortunately this is less frequent than simple goitre, as it is attended by severe constitutional disturbance—intoxication—*toxic goitre*.

So far as is at present known, the exophthalmic goitres arise independently of iodin necessity, cannot be modified by iodin therapy, and seem to be characterized rather by disposition to deliver excessive quantities of iodin combinations into the blood than to collect and retain them in the thyroid gland.

Möbius, as early as 1887 first suggested that the exophthalmic goitre was toxic because it delivered too much of the thyroid substance to the blood—*hyperthyroidism*.

Experiments with the thyroxin, which Kendall believes to be the active principle of the thyroid secretion, show that its administration to those suffering from deficiency of thyroid substance—*hypothyroidism*—as in cretinism and myxedema, brings about rapid improvement in favorable cases, and that its excessive administration to normal individuals sets up a train of symptoms comparable to those seen in exophthalmic goitre—hyperthyroidism.

It is paradoxical that the development of simple goitre occurs when there is absence of and necessity for iodin, that the development of exophthalmic goitre occurs when iodin is present and is being delivered in excessive quantities into the blood, and that a few cases of exophthalmic goitre should improve upon the administration of thyroxin. Evidently knowledge of goitre requires further study and elucidation.

But this is not all: simple goitres, especially when nodular, and seeming to arise in the usual way, may either remain mere local disturbances, or suddenly or slowly acquire toxic qualities, and assume the characteristics of exophthalmic goitres. Thus it is made to appear as though the lesion that at one time arises through deficiency of iodin, may later become the seat of excessive iodin deposits.

This seems to depend upon what goes on in the nodule, in case it assumes the quality of a tumor and ceases to obey the normal economic physiological laws. So long as it is simply vegetative, there is only local deformity. Let it assume the function of secretion, and the patient becomes intoxicated.

Crile found that the removal of an adenoma from the enlarged thyroid of a patient with exophthalmic goitre relieved the toxic symptoms just as a host of surgeons have found that removal of a part of the gland relieves the symptoms in about 80% of the cases. Adenomas occur in about 20% of toxic goitres and may explain the symptoms in those cases. But the remaining 80% are without nodular formations and depend upon misbehavior of the gland itself.

As a rule the symptoms of hyperthyroidism arising in cases with adenomas make their appearance late. Plummer asserts that it appears ten years later than in cases without nodular formations, and that it lacks the exophthalmos so characteristic of the simple enlargement.

When any goitre becomes toxic—i.e., develops the characteristics of the exophthalmic goitre—the surgical aspects of the case at once change.

In simple goitre what the patient seems to need is more thyroid substance, therefore there can be no logic in removing the gland, as that only diminishes what he has; but in exophthalmic goitre, he has too much thyroid substance, and may be helped by the removal of the source of the excess. Of course it is important not to remove the entire gland less cachexia strumipriva supervene.

It must be evident to the reader that the inexact state of knowledge of the subject precludes the possibility of scientific classification of goitres.

Langhans, followed by Quervain, and later by Berard and Alamartine, impressed with the importance of the embryonal elements in the thyroid, evolved a kind of embryological classification, as follows:

    I. Tumors of Mesobranchial Type.—These are supposed to be derived from the thyroglossal duct, from which the greater part of the thyroid is developed.
        A. Congenital median cysts and fissures of the neck and malignant tumors resulting from their degeneration.
        B. Cylindrical cell goitres and perhaps myxomatous goitres.
        C. Benign goitre.
        D. Malignant goitre.
        E. Aberrant benign goitre.
        F. Aberrant malignant goitre.
    II. Tumors of Branchial Type.—
        A. Of ectodermic origin—cancer of the thyroid with squamous epithelium.
        B. Of endodermic origin—benign or malignant parathyroid tumors; benign or malignant thymic tumors—struma ultimobranchiale maligna of Getzowa.
        C. Of mixed origin—mixed tumors, embryomas, terratoma of the thyroid body.

Okinczyc has devised a much more elaborate classification in which a number of different characters are employed:

    I. According to their situation, goitres are divided as follows:
        A. Enlargements of the thyroid body itself.
            (a) In the normal position of the gland.
            (b) In an abnormal position.
                1. At the supra-sternal notch ("goitre plongeant").
                2. Retro-clavicular— ⎫
                                 ⎬ Endothoracic.
                3. Retro-sternal ——— ⎭
        B. Enlargements of the thyroid structure, either entirely separated from the thyroid gland, or connected with it by a pedicle.
            4. Mediastinal.
            5. Retro-pharyngeal.
            6. Lingual.

7. Endopharyngeal.
8. Endotracheal.
II. According to the extent of the enlargement:
    A. Partial,
       Affecting the isthmus or one of the lateral lobes, or the isthmus and a lobe.
    B. Total,
       Affecting the whole body of the gland.
III. According to the character of the enlargement:
    A. Diffuse,
       Characterized by uniform enlargement of the thyroid.
    B. Nodular.
       Characterized by the presence in the otherwise normal thyroid, of nodules of tissue
         of varying type, surrounded by more or less distinct capsules.
IV. According to the character of the morbid changes observed.
    A. Benign goitres.
       (a) Adenomatous.
          1. Of thyroid structure:
             *Small acinous adenoma.
            **Pale cell adenoma.
           ***Colloid adenoma.
           ****Malignant adenoma.
          2. Of para-thyroid structure:—Parastruma (Langhans).
            *Intra-thyroid.
           **Extra-thyroid.
       (b) Colloid.
       (c) Cystic.
       (d) Fibrous.
       (e) Calcific.
       (f) Vascular.
    B. Mixed tumors of the thyroid.

Wullstein and Wilms, and Wullstein and Kuttner, base their classification entirely upon the morbid anatomy of the goitres:

Struma benigna.
    I. Struma diffusa.
       A. Struma follicularis (Struma parenchymatosa).
       B. Struma desquamativa (the goitre of Basedow's disease).
       C. Struma colloides.
    II. Struma nodosa.
       A. Struma follicularis (so-called adenoma).
       B. Struma colloides compacta (conglomerate goitre).
       C. Struma colloides cystica.
    III. Mixed varieties.

L. B. Wilson classifies the goitres clinically and physiologically, using the intoxication of hyperthyroidism as the chief character:

Goitre
    I. Hyperplastic toxic goitre—exophthalmic goitre.
    II. Non-hyperplastic toxic.
       A. With high blood pressure.
       B. With low blood pressure.
    III. Non-hyperplastic questionably toxic.
       With low blood pressure.
    IV. Non-hyperplastic non-toxic.
       With low blood pressure.

It is evident that while such a system may be of some clinical value, it is of no pathological value, for it tells very little more about the goitre than that the patient has one. It also seems to make no allowance for the fact that though certain goitres are primarily toxic, others are secondarily so.

For our present purposes, a goitre is a tumor-like swelling, taking the place of the thyroid gland, attached to the larynx and trachea, and rising and falling with the movements of deglutition.

FIG. 258.—Unusually large cystic goitre. (*Coplin.*)

Such enlargements vary from simple increased visibility to a great size.

They may be symmetrical and uniform, or asymmetrical and nodular. In some cases they involve the entire gland, in others only the median lobe or isthmus; sometimes a lateral lobe, sometimes the isthmus and a lateral lobe.

When removed from the body by dissection, and examined with the naked eye, the normal thyroid is found to be composed of an almost uniform substance of a reddish brown or brownish amber color, divided up by numerous whitish or grayish bands of connective tissue forming a reticulum, and constituting

the fibro-vascular framework of the organ. About the whole there is a well-developed capsule.

Small diffuse goitres do not differ essentially in appearance from the normal structure. The enlargement considered characteristic of exophthalmic goitre, which is also a diffuse goitre, and usually not a large one, commonly differs in having a paler color, and a less translucent substance. But there is no constant or characteristic naked eye appearance by which the exophthalmic goitre can be recognized.

The nodular goitres are entirely different, and present a great variety of appearances that are somewhat bewildering to those not familiar with them.
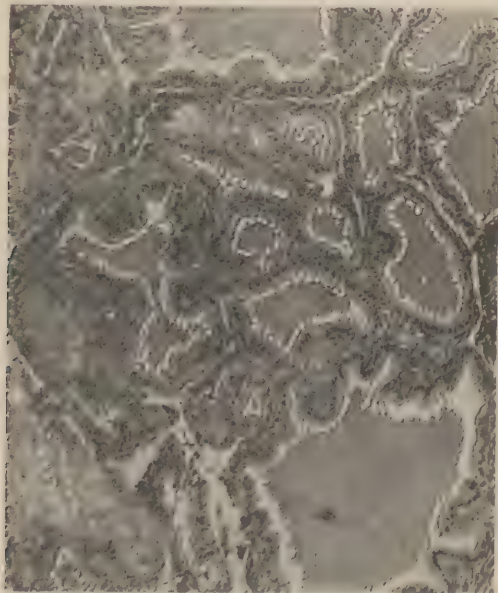
Fig. 259.—Photomicrograph of a section of thyroid (×120). Type C. Regressing primary parenchymatous hypertrophy and hyperplasia. From a case of clinically true exophthalmic goiter; late stage. (*L. B. Wilson.*)

They may contain a single nodule, several nodules, or be made up of a conglomerate mass of nodular formations of varying size and appearance.

As a rule each nodule is well circumscribed, and usually encapsulated. It may be of a color and general appearance corresponding with that of the thyroid itself, or dark, almost to blackness, or pale, pinkish or grayish, or mottled dark and pale. Some are reasonably firm, though they lack the fibro-vascular trabeculae of the normal organ, some soft, some almost fluid. Nodules of various color and consistence may co-exist in the same thyroid.

The causes of these differences are not difficult to understand upon the basis of their probable origin. If they originate from the vestiges of embryonal tissue, the stage of development to which they have arrived may be looked upon as the primary source of difference. The nodules that represent rapid growth of alveoli, and in which because of the rapidity of growth, they remain small, will

be pale in color and relatively dense in substance, while nodules of less rapid formation, and in which colloid collects, will be more of the normal appearance, and others in which the colloid collects in excess will be softer and more yellowish. Those nodules in which much colloid accumulates may become cystic, and as the collection becomes greater and the distension of the alveoli increases, the interalveolar walls may rupture and larger and larger cysts form until spaces several centimeters in diameter filled with amber colored jelly may be found. Complicating disturbances sometimes supervene upon these simple changes and bring about new conditions. Thus, sometimes hyaline or mucinoid change of the inter-alveolar connective tissue occurs and may eventuate in the melting away of the supporting connective tissue framework, and the suspension of the alveoli in a semifluid matrix.

Not infrequently hemorrhages occur into the embryonal tissue formations, giving them a deep red color as far as the infiltration of blood extends.

In old goitres the connective tissue framework suffers from proliferative and retrogressive changes. Of these fibrosis is one of the most common, bringing in its train calcification and in rare cases ossification of the stroma.

If the structural variations of the same chronic goitre could be followed from day to day, it might be possible to show that the conditions described are more or less in regular sequence, but of course this cannot be done.

We do not feel that much stress is to be laid upon the described differences, yet as has already been shown they are frequently used as criteria for classification.

The histological variations in general correspond to the macroscopic appearances. They are even more frequently used as bases of classification than the gross appearances,

When there are no nodules in the thyroid body, and it is diffusely enlarged without considerable variation from the normal type of structure, the condition is described as *non-hyperplastic goitre, parenchymatous goitre, struma parenchymatosa*, or *struma follicularis*. If these cases become toxic, i.e. develop into exophthalmic goitres, the colloid substance becomes fluid and is absorbed, while the epithelial cells proliferate and many of them desquamate.

The epithelial linings of the alveoli become thrown into folds or plicae, which in sections look not unlike buds or excrescences from the walls. This appearance characterizes the *hyperplastic goitre* or *struma diffusa desquamativa* and is the chief microscopic characteristic of the *exophthalmic goitre* or goitre of Basedow's disease.

But if instead of the colloid becoming absorbed and disappearing and the epithelial cells proliferating, the alveoli harbor an increased quantity of colloid, the goitre, rarely toxic, is known as *struma diffusa colloides*.

If a thyroid that has been enlarged through accumulation of colloid later loses the secretion, its connective tissue appears to be increased, and it becomes smaller and firmer, *struma fibrosa*.

In some cases the vessels of the goitre are excessively large—*struma vasculosa*.

The nodular form of goitre is almost universally spoken of as *adenoma*. If the nodule or adenoma is chiefly composed of minute alveoli, it is sometimes

called *fetal adenoma* or *small acinous adenoma*. If it be composed of alveoli of about normal size, it is frequently spoken of as *parenchymatous adenoma*.

If the cells of such an adenoma be unusually pale—a condition which no one seems to understand at the present time,—it is described as "*adenoma with pale cells.*" If they produce more than the usual amount of colloid, and the secretion accumulates, it is known as *colloid adenoma*.

FIG. 260.—Photomicrograph of a section of thyroid (×120). Type E. Fetal adenoma. From a case of clinically toxic non-exophthalmic goiter. (*Wilson.*)

The chief microscopic difference between the structure of the gland proper and its adenomatous nodules is the presence in the former and absence from the latter of well-developed fibro-vascular trabeculae.

MALIGNANT DISEASE OF THE THYROID GLAND

It is inevitable that there should be confusion between goitres and tumors, seeing that in so far as the nodular form of goitre is concerned, the nodules are tumors (adenomas). So soon, therefore, as the surgeon removes a goitre and discovers a nodule or nodules, he desires to know what kind of a tumor the nodule is, and above everything else, whether it is malignant or benign in nature. Ninety per cent of the malignant tumors of the thyroid are thought by Crile to originate in adenomas. There is, however, no way to check the statement. They probably originate as nodules.

One would suppose that malignancy ought to be easily determined by a microscopic examination of the specimen, but this is not always true of the tumors of the thyroid. In very rare cases they are said to show typical histolo-

gical structure, with normal appearing alveoli, the epithelial cells of which are all perfectly held in normal bounds by their basement membranes, yet are found to be metastatic in the flat bones and in the lymph nodes. As in the metastases the same normal arrangement of epithelial elements is preserved, it seems less correct to describe them as cancers or carcinomas, than as *malignant adenomas*, or *metastatic colloid struma*. No case of this kind has come under our observation, and Porter, saw none in his series of 139 cases of goitre.
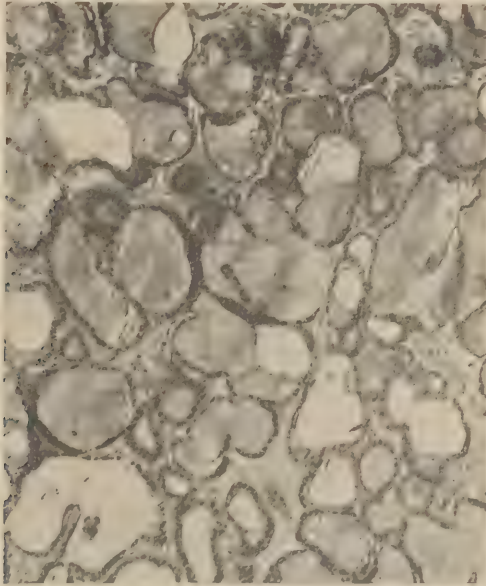
FIG. 261.—Photomicrograph of a section of thyroid (×120). Type G. Adult, "colloid" adenoma. From a case of clinically toxic non-exophthalmic goiter. (*Wilson.*)

The matter of diagnosis is further complicated by the fact that occasional thyroid tumors with atypically arranged epithelial structures, bearing more or less complete correspondence with the microscopy of carcinoma, as it is seen in other viscera, are clinically benign.

The number of malignant thyroid tumors is not great. In the Mayo clinic 1.19%; in the experience of Ochner and Thompson 1%. Pörter found five cases out of 139 to be malignant—3.64%.

An idea of the appearance and conditions observed among the malignant thyroid tumors may be gathered from the following tabulation from Wullstein:

Struma Maligna.
  Sarcoma.
  Carcinoma.
    Metastatic colloid struma—the structure appears typical in histological arrangement, but is metastatic in the lymph nodes, and in the bones.
    Adeno-carcinoma—histologically like carcinoma, especially at the periphery, but not tending to penetrate the capsule. Rarely metastatic, and when so, the secondaries are like those of metastatic colloid struma.

FIG. 262.—Photomicrograph of a section of thyroid (×120).   Type H.   "Colloid thyroid."
From a case of clinically non-toxic goiter.   (*Wilson.*)
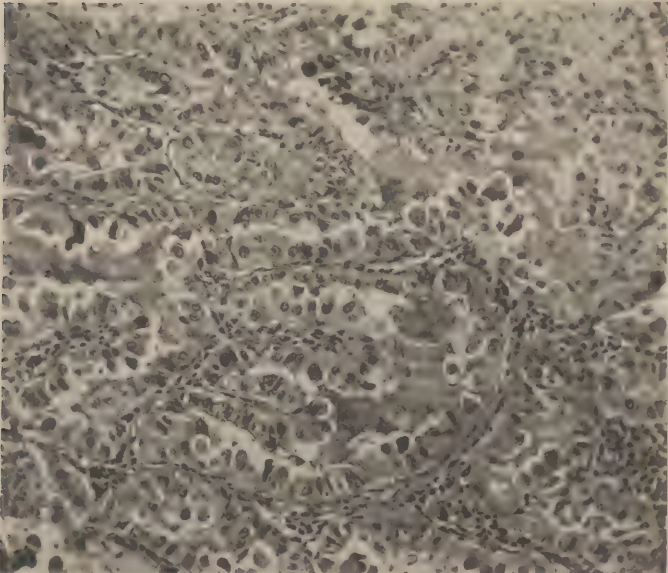
FIG. 263.—Malignant papilloma of the thyroid. The papillae bear large functioning cells (see colloid and surrounding clear spaces), with sharply staining nuclei and mitotic figures. Malignant papilloma. (×100.) (*Wilson.*)

Papilliferous cystoma.

Carcinoma—differing from the adenoma in that there is a distinct tendency to penetra-
tion of the capsule, and invasion of the neighboring tissues, with metastasis.

Small alveolar, large cell struma—composed of large cells rich in protoplasm, arranged
in alveoli or in columns, and supposed to arise from the post branchial bodies of
Gezowa, the source of the rudiments of the lateral lobes of the thyroid.

Parastruma maligna—composed of polyhedral or columnar groups of cells sometimes
in alveoli, of a remarkably pale appearance, and rich in glycogen. Langhans is of
the opinion that they are traceable to the parathyroid bodies. They are metastatic.

Squamous cell carcinoma—supposed to arise from vestiges of the thyro-glossal duct,
or of the branchial clefts.
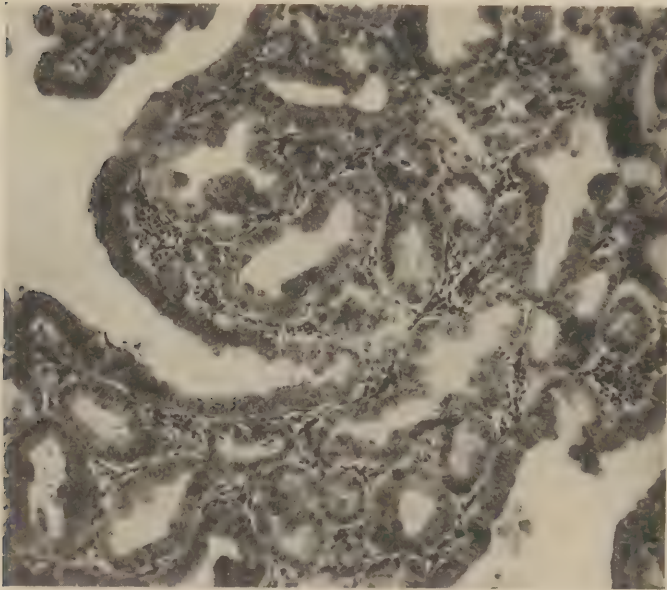
Fig. 264.—Non-malignant papilloma of the thyroid. High columnar epithelium with small
nuclei; no mitosis. Non-malignant papilloma. (×100.) (*Wilson*.)

In the section upon tumors it has already been pointed out that the differen-
tiation of sarcoma and carcinoma, so simple upon theoretical grounds, is fre-
quently difficult in practice. In the case of the thyroid gland it appears to be
exceptionally so, and it may be stated without much reservation that the more
carefully the tumors are studied the less frequently is the diagnosis of sarcoma
made by competent histologists. Among the earlier writers, resemblances were
pretty generally accepted as facts, so that tumors of the thyroid of highly
cellular structure and theoretical resemblances to the sarcomas of other viscera
were unhesitatingly classed as such. It is probably on this account that Ehr-
hardt was able to collect 99 sarcomas of the thyroid as well as 150 carcinomas,
though later writers place the incidence of sarcoma as about one to three or four
carcinomas.

26

L. B. Wilson of the Mayo Clinic, found the following proportions:

MALIGNANT TUMORS OF THE THYROID

	MALES	FEMALES	TOTAL
Carcinoma, operated on	24	38	62
Carcinoma (?) not operated on	29	54	83
Malignant Adenomas	19	83	102
Malignant Papillomas	9	15	·24
Sarcomas	8	11	19
Total	89	201	290
	31%	69%	

FIG. 265.—Microscopic section of a carcinoma of the parotid gland. (*Photomicrograph by Prof. Allen J Smith.*)

Wilson states that the number of cases of malignant tumors of the thyroid which have been detailed in the literature to Aug. 1921, is probably not more than one thousand. These he tabulates as follows:

MALIGNANT TUMORS OF THE THYROID CONCERNING WHICH INFORMATION IS AVAILABLE

Source of information	Epithelial	Sarcomas	Unknown	Total
Müller and Speese (summary to 1906)	181	118	...	299
Literature 1906 to 1920	524	39	109	672
Reported in personal communications to the author by 67 American surgeons, Jan. 1, 1917	98	19	52	169
Mayo Clinic cases, Jan. 1, 1905 to Jan. 1, 1917:				
Positive	115	19	83 not operated on	290
Doubtful	73			
Total	991	195	224	1,430

As the result of the data collected, and his own experiences, the author of the paper continues

"Much of the common impression that malignant tumors of the thyroid are relatively rare, is believed to be due in part at least to the high percentage of error in the diagnosis. In the Mayo Clinic, of the 97 patients operated on who have died of the disease or who when heard from last were known to have undoubted recurrences, usually metastatic, there were 50 whose clinical histories before the first operation contained no suggestion of malignancy. The glands removed at operation from all of the 97 were examined pathologically, yet at the first operation
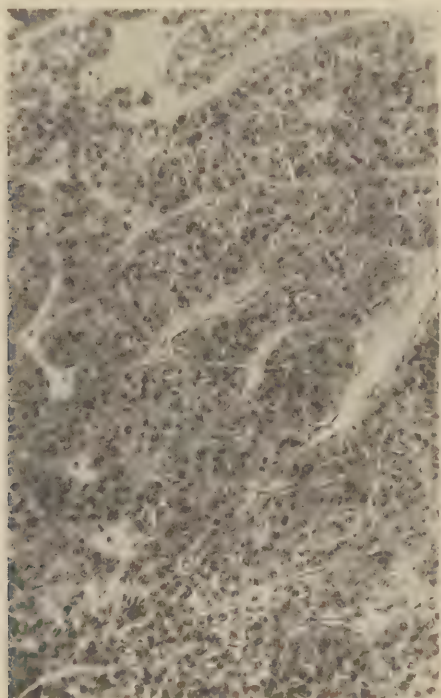
FIG. 266.—Adeno-medullary carcinoma of the thyroid. A section through the softer portion of tumor showing large epithelial cells proliferating and degenerating lying in well-marked cordons and follicles. The character of cells indicates the beginning medullary type. Arrangement shows plainly adenomatous origin. (×100.) (*Wilson*.)

23 of these were passed by the pathologist without a suspicion of malignancy. It is believed that in the last three or four years the percentage of accuracy of diagnosis both clinical and pathologic has been very greatly increased in the Clinic but it is too early to obtain complete mortality statistics in the cases. It is suggested that surgeons should follow up their patients operated on for adenoma of the thyroid, especially after the lapse of three or four years, in order to determine the incidence of death from or recurrence of tumors the malignancy of which was not suspected at the time of operation."

"Aside from hyperemia and inflammatory deposits, thyroid enlargements, as met at operation and necropsy, are directly due either to storage of secretion or proliferation of tissue or both. If due to storage of secretion, they are colloid goitres. If due to diffuse proliferation (hyperplasia of normal adult tissue which hyperfunctionates, they are exophthalmic goitres. If due to circumscribed proliferation of (usually embryonal) parenchymatous tissue, they are adenomas. If these adenomas remain perfectly encapsulated and if they cease to

proliferate and gradually degenerate, they are "benign" in the sense that they do not invade surrounding structures and do not metastasize. They may, however, cause untoward local symptoms from pressure and they may be associated with a symptom syndrome, the chief characteristic of which is usually a slowly developing hypermetabolism with cardiac disturbances but rarely with exophthalmos, a syndrome which H. S. Plummer designates "Toxic non-ophthalmic goitre" or "toxic adenoma." If adenomas continue to proliferate rather than degenerate they may penetrate their capsules, invade the other portions of the gland or surrounding structures and metastasize, ultimately causing the death of the patient by destruction
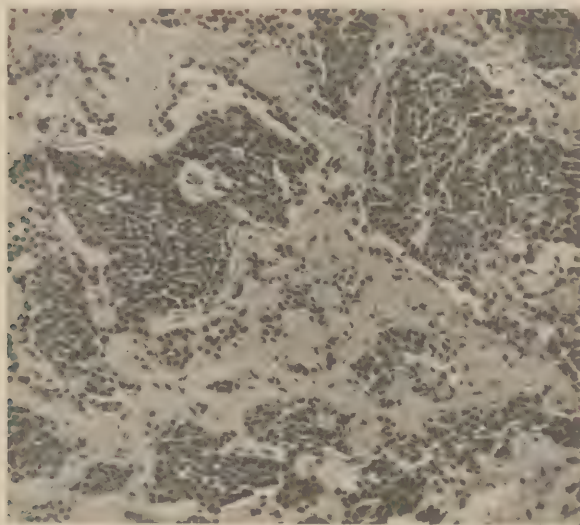
Fig. 267.—Scirrhus carcinoma of the thyroid. A section through a hard portion of the tumor in the thyroid, showing epithelial cells much condensed by fibrous connective tissue. Scirrhous carcinoma. (×100.) (*Wilson*.)

of either local or distant organs." These proliferating adenomas (the "wucherende Struma" of Langhans) thus may or may not be malignant and histologically it is almost impossible to differentiate the two. Broadly speaking the only reliable marks of distinction are the details which indicate the predominance of one or the other of the two processes, namely proliferation and degeneration. Again, broadly speaking, it follows from this that any sizable adenoma of the thyroid composed of embryonal tissue in a person of cancer age which histologically shows that it is in active proliferation is potentially malignant even though it is still contained entirely within its capsule."

"Neoplasms of the thyroid composed of adult parenchymatous cells, if encapsulated, always suggest having been derived from embryonal tissue during post natal life though by no means can this always be proved. Langhans considers them late stages of "wucherende Struma."

"Such encapsulated masses of large adult parenchymatous cells, while frequently arranged in acini resembling those of the normal thyroid, are more frequently the subject of extensive degeneration. And such degeneration may be sufficiently extensive to produce sloughing or broken down areas. The epithelial cells adjacent thereto are large, often with hydropic cytoplasm and relatively small nuclei. The parenchyma is not infrequently markedly papilliferous. Such adenomas composed of epithelium, apparently adult in all respects, are associated with clinical conditions parallel with those mentioned as coincident with adenomas of embryonal type. They may cause only local pressure symptoms, they may be associated with the syndrome of toxic adenoma (Plummer) or they may invade surrounding structures and metastasize to distant organs thus placing them in the class of malignant neoplasms.

They are undoubtedly the origin of that group of malignant tumors usually designated adenocarcinomas."

"Occasionally there is met with an aberrant diffuse proliferation of parenchyma of the thyroid with little or no evidence of the formation of normal secretion or of the storage of colloid, and without evidence of encapsulation except the normal capsule of the entire lobe. It is believed that such tumors may exist without causing other than local symptoms and these but slight. I have seen not more than ten or fifteen of these in my entire experience. On the other hand, solid homogeneous non-functionating aberrant proliferations of the thyroid are almost always neoplasms which invade surrounding structures and metastasize to distant organs. While in one sense these are adenomas, for the sake of clearness, let us leave out of account their suggestion of nodular encapsulated neoplasms and refer to them simply as carcinomas of the thyroid."

FIG. 208.—Spindle-cell sarcoma of the thyroid. A section through a solid area showing spindle-cell sarcoma with a few round cells. (×100.) (*Wilson.*)

All other tumors of the thyroid associated with symptoms of malignancy are usually described as sarcomas. Beside their connective tissue elements in which any form of sarcoma cell may be the dominant one, although it is most frequently the spindle cell type, there are also almost invariably present, large or small groups of parenchymatous cells which show that they are also proliferating. Whether or not the neoplastic process started with the parenchymal elements or whether the process was from the beginning a proliferation of the connective tissue elements with only secondary stimulation of the parenchymatous cells as they were gradually squeezed out, it is impossible to say. There is usually a history of recent rapid development, and the prognosis of the early demise of the patient must be made. We must continue to call these tumors sarcomas whatever may be our hypothesis with regard to their epithelial or mixed origin."

"Of the 290 patients in the Mayo Clinic, 158 had developed goitre before they were 30, and 106 in the next two decades. One hundred and fifty nine patients had had thyroid enlargement for five years or more. Only 61 patients had not noticed thyroid enlargement previous to one year before a diagnosis of malignancy. It is probable that a malignant neoplasm of the thyroid may exist for a considerable period without causing pressure or other

symptoms which compel the patient to seek medical advice. It is usually difficult to elicit a history of definite onset of symptoms referable to malignancy as distinguished from symptoms referable to the presence of a supposedly benign tumor of the thyroid. Usually the first
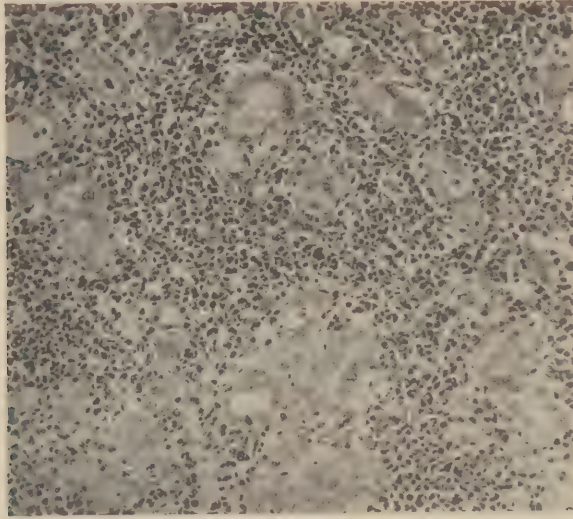
FIG. 269.—Carcinoma sarcoma of the thyroid. A section through the edge of the tumor, showing proliferated epithelial cells which are now degenerating, and proliferation of connective-tissue cells between the acini. Carcinoma sarcoma. (×100.) (*Wilson.*)
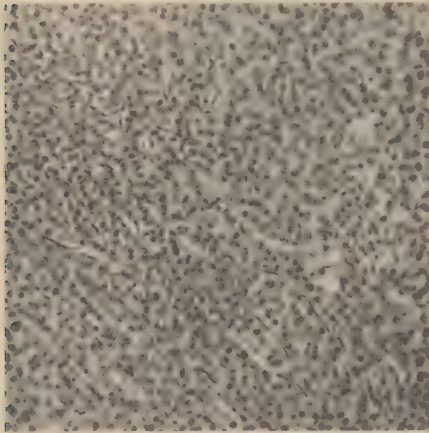
FIG. 270.

FIG. 271.

FIG. 270.—Fetal adenoma of the thyroid. A section through the dense portion of the adenoma immediately under the capsule. Note small embryonic cells arranged in lobules and bands with a very small amount of stroma (thin-walled blood vessels) between. (×100.) (*Wilson.*)
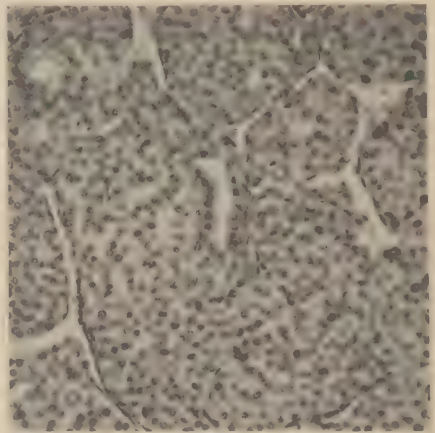
FIG. 271.—Fetal adenoma of the thyroid. A section from an area farther from the capsule than that shown in Figure 270. The embryonic cells are larger and in larger lobules, marked off by cleft-formed blood vessels. (×100.) (*Wilson.*)

symptom leading to the suspicion is an increase in size of the gland at a rate greater than that which has continued for some years. Yet this increase growth rate is rapid in only about one third, and slow in the remainder. Growth usually progresses steadily and without periods of

regression in size such as are usually seen in thyroid enlargements of inflammatory origin. Of the total number of patients examined in the Mayo Clinic about one fourth had noticed symptoms of continuous growth for one year or less, and about one third had noticed symptoms of continuous growth for ten years or more. It may be doubted whether the process in the latter was malignant from the beginning of the continuous period of growth."

"The surface of a malignant thyroid is more apt to be irregular and nodular than when the enlargement is due to inflammation."

"They are, however no more irregular or nodular at the beginning than are non-malignant adenomas."

"Metastatic deposits are most frequent in the lungs. The skull, brain and liver are also frequent sites. A few cases have been reported of malignant tumors of thyroid tissue in organs distant from the thyroid in which necropsy revealed no evidence of malignancy in the thyroid itself."

THE MAMMARY GLAND

The mammary gland is an organ whose evolution and involution; masculinity and femininity; quiescence and activity; juvenility and senility, are characterized by such distinct histological structural variations as to puzzle those unfamiliar with the details, and not infrequently lead them to mistake that which is entirely normal for indication of disease. On this account it is of the utmost importance for the surgical pathologist to familiarize himself with all of the data in our possession relative to the normal gland.

In 1892, O. Schultze pointed out that at an early period of embryonal development, slight ectodermal ridges can be found passing along each side of the body

FIG. 272.—A series of embryo pigs showing the milk line, and its breaking up into the mammary rudiments.

from the axilla to the groin, and to them he gave the name "Milchleisten" or milk-lines. Later observers confirmed the observation and Kallius and Brouha showed it to be as true of human embryos as for those of lower mammals. When the embryos attain a length of 20 60 mm. the lines become broken up into a series of points, or minute accumulations of ectodermal cells each of which is the rudiment of a future mammary gland. According to the species, all, or some of these survive and develop, or many of them disappear. Thus, Schickele found that there were ten of them in the embryo guinea-pig, though only two, in the inguinal regions, finally developed. In man all become extinguished except two in the pectoral region.

Whether an individual will possess the number of mammary glands normal for his species, therefore depends in part upon the extinction of the superfluous and the development of the appropriate rudiments. If all are lost, there will be

no mammary glands—*amastia;* if too many are retained, there will be super-numerary glands—*polymastia.*

In human beings amastia is extremely rare, and a careful review of the litera-ture reveals only five cases, four in women, and one in a man, on record. Uni-lateral amastia, which may sometimes depend upon the same cause, but which seems in nearly all cases to depend upon entirely different causes, such as the pressure of the arm of the fetus upon the breast while in utero, with resulting atrophy and disappearance of the once developed organ, is not included. Of such cases the literature contains about fifty cases.

Of the other condition, polymastia, the reverse is true, and more than ten thousand cases are referred to in the literature of all countries. The super-

FIG. 273.—Complete bilateral amas-tia, a condition of which there are only six cases on record. (*Wylie.*)

FIG. 274.—Unilateral amastia. In this case it is said that there was no muscular or other atrophy of the defective side as is usual. (*Launois and Hubert.*)

numerary organs for the most part occur along the milk lines, any where from the axilla to the vulva, sometimes symmetrically, sometimes otherwise, in both sexes. The largest number seen was by Neugebauer, whose patient had eight supernumerary glands, making ten altogether.

Some of the supernumerary organs are very small, seeming scarcely to con-sist of more than a very small nipple; indeed they are sometimes described as "supernumerary nipples," but experience shows that in every case in which there was a nipple, a gland was situated beneath it. In the axilla supernumerary mammary glands frequently lack nipples, and may be without outlets; they are then frequently mistaken for adenomas. The axillary glands form an ascending series—outlets without nipples, outlets with rudimentary nipples, axillary mammae with well-formed nipples.

In addition to these milk-line glands, the literature contains a number of interesting cases in which the glands have occurred upon the mid-line of the thorax and abdomen; over the anterior superior spinous process of the ilium in the flank; on the buttock; on the upper arm; on the face; on the back of the neck, and on the hip. These are with difficulty harmonized with origin from the milk-line series, and have not yet been satisfactorily explained.

In some cases the supernumerary gland is situated within the confines of the normal breast, so that it appears to have two nipples; one is always above or below the normal full sized nipple.

Supernumerary mammary glands may or may not be useful according to their size. Many women have supplemented the nourishment of their infants by letting them nurse from the additional organs with which Nature had provided them. For the most part, they are much too small, and then are more or less of a nuisance, as not being emptied, and always secreting during lactation, they leak milk upon the clothing. They also sometimes undergo painful enlargement. It is sometimes recommended to excise supernumerary mammary

FIG. 275.—Diagram showing the various positions at which supernumerary mammary glands have been observed along the milk line. (*Stratz.*)

FIG. 276.—Polymastia. The supernumerary glands are in each axilla. (*Kayser.*)

glands lest they become the seat of tumors though there seems to be no other ground for this recommendation than the general fear of mammary tumors. It is not worth while to bother about them unless they distress the patient as the axillary glands without outlets sometimes do when they swell greatly at the beginning of lactation, and cause pain, or when those with outlets soil the clothing with milk.

Polymastia must be differentiated from *polythelia*, or supernumerary nipples. The latter results from imperfect development of one mammary rudiment, not from two, and the supernumerary appendages are not regularly placed one above the other, but are distributed otherwise. As many as five good sized and well-formed nipples have been observed upon one breast.

Returning, now to the normally situated primitive rudiment from which the mamma is to develop, it is found at first to consist of nothing but a thickening of the ectoderm, which depresses the subjacent tissues as well as projects above. As time passes, the growth below the surface exceeds that at the surface and the cells form a rounded mass that descends more and more deeply, and extends a
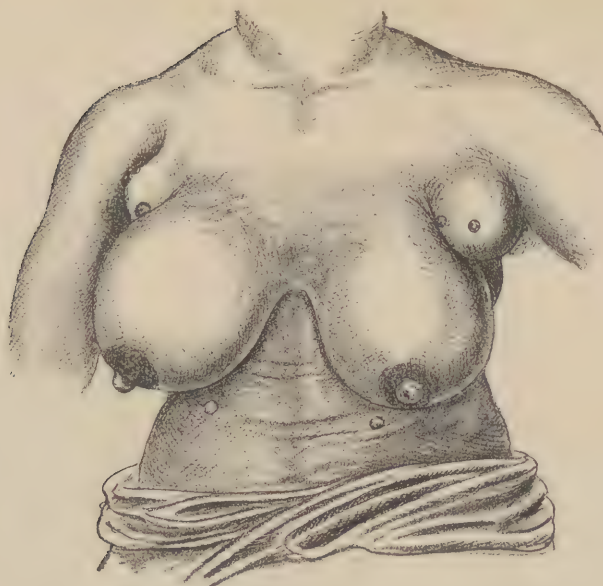
FIG. 277.—Polymastia.   Colored woman with nine mammary glands.   (*Hirst.*)

FIG. 278.—A case of polythelia observed by Dr. Fist in the Philadelphia General Hospital. In cases like this, in which the supernumerary nipple and areola are superimposed along the mammary line, the breast may really be developed from two of the mammary rudiments, the larger including the smaller.   It is then polymastia rather than polythelia.

little more widely, slightly elevating the developing skin on each side, and pushing its way laterally by buds, at first short and blunt, but later longer and more slender. As this stage is reached the surface usually becomes depressed at the center, where a dimple remains for some time after birth. Conditions differ at birth; in some cases there is no nipple, in others a very rudimentary one. But it never projects; it is always either flat or slightly depressed.

Two or three days after birth, the breasts of infants of both sexes enlarge and show the first signs of secretory activity. It is supposed that the stimulation is derived from the colustrum, or early milk of the mother, which contains the hormone or internal secretion that excites her breasts to action, and thus finds its way into the blood of her infant. Whether this is so or not ought to be discoverable through observations made upon infants never applied to the maternal breast. If they manifest the same secretory enlargement, it must depend upon something intrinsic in them, or upon the external frictional contact with clothing, etc. It is

Fig. 279.—Polythelia. Two nipples of nearly uniform size upon the right breast. (*Bartels.*)

rare, however, that one has an opportunity to observe an infant never applied to the maternal breast.

The infantile breast swells to a size that varies in different cases, sometimes enlarging very little, so that secretion would not be suspected if not looked for, sometimes projection as a distinct hemispherical organ as large as a walnut. The swollen organs are usually tender, and for that reason the condition has entered the literature under the name *mastitis neonatorum*. There is, however, no inflammation; the disturbance resembles that experienced by the mother, whose breasts also swell and become painful at about the same time.

When the little organs are gently pressed a cloudy fluid exudes—"witch's milk." Upon microscopic examination it is found to resemble the columstrum of the maternal breast, and like it, contains varying quantities of fat. In some cases it is very watery, in others distinctly milky.

It is partly the result of vacuolation and degeneration of the centrally situated cells of the epithelial processes, and secretion by the others, and results in the permanent canalization of the epithelial processes of the developing gland, which thus become transformed into the future ducts. There are no acini. A section of such a gland shows it to be composed of an aggregation of more or less widely dilated spaces, lined with fairly regularly distributed cuboidal epithelial cells, many of which contain fat globules, and filled with the fluid already described.

In the course of some ten or more days, secretion ceases, the breasts gradually diminish in size, and again become flattened. Microscopic examination shows
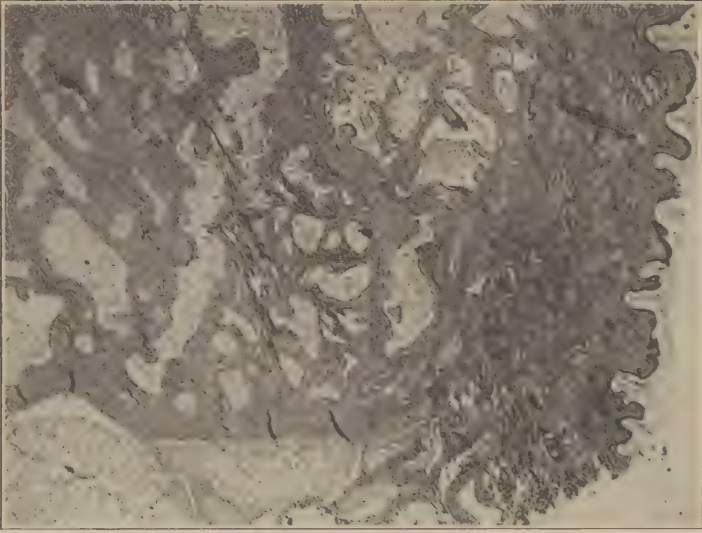
FIG. 280.—Microscopic section of the breast of an infant aged three weeks, dying in the Philadelphia General Hospital, and not yet recovered from the period of primary activity and the secretion of "witch's milk." Note that there are no lobules or acini. The secretion results from activity in the cells lining the ducts, which the low magnification does not permit to be seen.
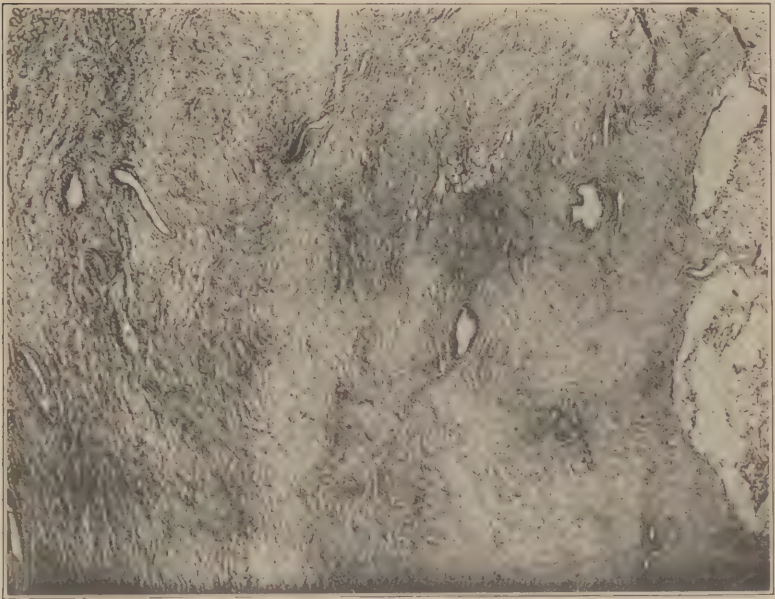
FIG. 281.—Microscopic section of a normal male breast, taken at autopsy from the body of a white man aged 38 years dying in the Philadelphia General Hospital. The structure and the proportion of parenchyma to stroma are almost identical with that of the female before pubrety.

that the dilated epithelial spaces have retracted and are empty, but remain canallated and duct-like in appearance.

From this time until adolescence there is very little visible change in the breast of either sex, yet in both sexes the structures are developing both internally by the gradual augmentation of the epithelial structure, and externally by the gradual development of the papilla that is the beginning of the nipple, and by the differentiation of the areola.

With the advent of puberty, the breasts of both sexes undergo additional development, but that of the female greatly exceeds that of the male, which is not infrequently overlooked. In both sexes the epithelial structure or, as it must now be called, the parenchyma, increases, but in the female, the stroma increases to a much greater degree.

In the male the epithelial structures that correspond with the ducts of the female breast, descend for a slight distance, into a slightly modified fibrillar tissue beneath the skin radiating in all directions from the nipple, and terminating without sharp limits. The areola becomes perfected, and the nipple is completed. While this goes on there is sometimes a small amount of secretion that can be expressed from the parenchyma. In very rare cases the evolution of the organ does not stop here as is normal, but progresses precisely as in the other sex, with resulting female organs on the thorax of the male. Such a condition is known as *gynecomastia.*

Although most frequent during adolescence, the development of gynecomastia is not limited to that time. The male breast is a mammary gland, though of small size, and at any time it may be aroused, much as the female gland can, to enlarged size and glandular growth, and even to lactate. From the literature it has been possible to collect 162 cases of this anomaly, illustrating every stage from simple moderate enlargement, to complete lactation hypertrophy, in which the male breast assumed a size and importance equalling that of the female breast.

Gynecomastia should not be looked upon as an anatomical change; it is physiological, and the enlargement is a hypertrophy. It is in no way injurious, and no apprehension of subsequent evil need be feared. In some cases the breasts have been amputated upon suspicion of impending tumor development,

Fig. 282. Gynecomastia. The Zulu chief Chengwayo, who had 40 wives and more than 100 children, some of whom he partly nursed at his own enormous mammae. (*Schufeldt.*)

but there is no relation between the two. But care should be taken to make sure that an enlargement of the male breast is gynecomastia and not a tumor. In some cases this is not so simple as might at first seem, for in a few cases that

have come under our observation gynecomastia has developed irregularly, nodes first appearing, then fusing until symmetrical enlargement and the female appearance resulted. The nodules represented different glandular lobes undergoing successive hypertrophy. Quite a number of similar cases have come under our observation in which irregularly nodular male mammary glands have been amputated, but in which no tumor was present. They showed nothing abnormal upon microscopic examination, and the diagnosis usually made in such cases is "diffuse fibrosis," which is incorrect. In no case of gynecomastia thus far examined has there been lobular structure with acini such as occur in the female breast; the secretion is the result of activities that go on in the ducts.

Some patients with gynecomastia request the removal of large organs because of the feminine appearance of the chest which offends their manliness, and a few have been so mortified as to have performed the operation upon themselves.

In rare cases the female breast does not wait until the advent of puberty before developing, but proceeds to do so in infancy. The result is the occurrence of an adolescent or adult breast upon the bosom of a child

FIG. 283. Little girl of four and one-half years with precocious sexual development, and adult type of mammary glands. (*Mudd.*)

of tender years. This is extremely rare and occurs in association with precocious development of the other sexual organs, and the early appearance of menstruation. The literature contains about two dozen such cases. It is, of course, not the breasts that are at fault, but the endocrine system, functioning prematurely. No microscopic examinations of such breasts seem to have been made, but there seems to be no reason to suppose that they should in any differ from breasts developing at the normal time.

The normal development of the female breast at puberty remains to be described.

At the opening of this era, the breasts of female children are a little larger, and the nipples distinctly larger and more prominent than in males.

The first signs of change usually appear beneath the areola, which gradually becomes protuberant, thrusting the nipple forward, the whole forming a little cone, the "Knospenbrust" of Stratz and other German writers. Shortly after, the surrounding skin and fascia become elevated by the fore-shadowing of the hemispherical elevation of the fully developed breast. As this increases, it is still surmounted by the little cone composed of the nipple and areola, so that the whole structure is in reality of conical rather than of hemispherical form. In some of the darker races, it always remains of that shape, but in Caucasians, at some time between the fifteenth and twentieth years, it assumes its final form through the development of firm connections between the milk-ducts and the

outer integument, an increase in the muscular tissue about the nipple, and the final contraction of these tissues by which the base of the small cone is contracted and the nipple drawn down upon the areola which becomes flattened, the breast thus acquiring its typical hemispherical form.

These external morphological alterations are the consequences of internal changes to which careful attention should be paid. Beneath the areola, where most of the glandular tissue—i.e., ducts—of the infantile breast were situated, the growth of the gland begins, hence the formation of the little cone. From this as a center, the tubular epithelial structures extend radially for a distance

FIG. 284.—Microscopic section of the normal breast of a colored girl of 12 years, dying in the Philadelphia General Hospital, and showing the extremely small amount of epithelial parenchyma, and the densely fibrillar structure of the stroma characteristic of the juvenile mammae.

corresponding to the circumference of the finally perfected breast, as long slender tubular duct-like structures, that branch more and more freely as greater territory has to be provided with parenchyma. It is frequently stated that the increase in the size of the developing breast is due to this forming parenchyma, but that is a mistake that can easily be shown by the microscopic examination of a number of virgin breasts. *The size of the breast does not depend so much upon its parenchyma, as upon its stroma.* And here an important matter is reached.

The stroma of the breast consists of the following different elements:

1. *The Interlobar Connective Tissue.*—This is a dense fibrillar tissue derived from the deeper fascias, and extending from the pectoral fascia upward toward the skin to divide the organ into some twenty or more lobes, indistinctly separated from one another.

2. *The Interlobular Connective Tissue.*—Each of the indefinite lobes of the mamma is composed of a great number of small units known as lobules, which constitute the chief bulk of the parenchyma, and about which much is to be said later. Separating them is a finer fibrillar tissue, of which the chief bulk of the mamma is composed.

3. *The Perilobular Connective Tissue.*—Surrounding each of the ultimate endings of the system of branching tubules—the so-called lobules of the breast—is a slightly denser connective tissue, not definitely differentiated from the interlobular connective tissue, but concentrically arranged.

4. *The Peri-ductal Connective Tissue.*—This is a loose fibrillar tissue that immediately surrounds each lobule, penetrates into its substance and separates the individual elements of the parenchyma. Of it more will be said further on.

5. *The Adipose Tissue.*—Derived from the general superficial fascia, enters the breast between the lobes, and becomes distributed between the lobules.

Now with these in mind, let their relations and proportions in the normal breast be investigated. Normal breasts of young virgins rarely come under examination. That they histologically resemble the breasts of older women seems to have been assumed, but without reason, and with resulting errors of interpretation.

The stroma or matrix of the breast of a young virgin is sometimes entirely fibrillar. If the girl be stout, and the thorax well covered with panniculus adiposus, the breast may also be covered with adipose, but the chief part is composed of a corpus mammae, which is fibrillar, and which appears under the microscope as a rather dense tissue. Sometimes section through the organ shows adipose tissue distributed throughout, the parenchyma occurring as white areas in the yellow fat. Naturally it is the glandular tissue that is wanted for study, and which is hence excised. When sections of this are cut and examined, it is almost invariable found to consist of fibrillar tissue without admixture of fat, or with occasional fatty vacuoles here and there. From this it seems that adipose tissue is present in the young virgin breast, only in the neighborhood of the interlobar connective tissue, and rarely enters the interlobular tissue.

But with the passage of years, the fat advances into the interlobular connective tissue until it reaches the lobules themselves, and in rare instances even penetrates into the periductal tissue.

We recently examined 124 normal breasts obtained from autopsies, to determine the quality of the stroma, with the following results:

Tabulation of 124 normal breasts, the average age of the women being 46.2 years.

    I. Stroma fibrillar only—11 cases, average age, 32.7 years.
        Extreme ages, 12 and 62 years.

    II. Stroma fibrillar and mucinoid—62 cases, average age, 42.6 years.
        Extreme ages, 17 and 85 years.

    III. Stroma fibrillar, mucinoid and fatty—48 cases, average age, 52 years.
        Extreme ages, 18 and 103 years.

    IV. Stroma mostly fatty—3 cases, average age, 58 years.
        Extreme ages, 34 and 81 years.

The mucinoid change was present in 110 cases, or 75%, the presence of adipose was noticeable in 113, or 80% of the cases.

In the breasts of ten virgins between 12 and 30 years, adipose tissue was present in the interlobular tissue of four only, and then only in very small quantity. In five of them no adipose at all was present in the interlobular connective tissue.

Here let it be remarked that the breast of youth is firm, elastic and protuberant, while the breast of age is soft, flaccid and pendulous, especially when lactation has occurred several times. The firmness of the juvenile breast depends upon its fibrillar tissue; the softness of the senile breast upon its adipose tissue.

But the juvenile breast, though firm is soft; not because of the fat it contains, but because of the condition of its fibrillar tissue which is nearly always more or less mucinoid. We are at a loss to know the precise nature of this
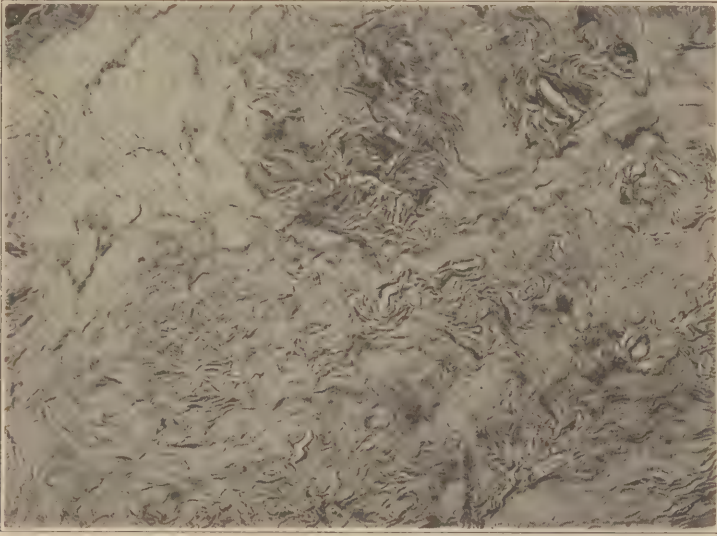
FIG. 285.—Microscopic section of the normal breast of a white woman aged 22 years, who died in the Philadelphia General Hospital. She had never been pregnant. The breast is almost without parenchyma, and its fibrillar stroma, almost without adipose, is distinctly mucinoid.

change described as mucinoid; it does not react like the ordinary mucins, and resembles the appearance of myxedema. It is present in quantities sufficient to be recognized in three-fourths of all breasts examined, and gives to the breast its peculiar elastic softness.

These not generally recognized structural peculiarities of the virgin breast, have given rise to the supposition that perfectly normal organs were the seats of pathological disturbance "diffuse fibrosis," chronic interstitial mastitis,"— or of vascular obstruction with mucoid degeneration.

The parenchyma of the virgin breast is no less subject to variation than its stroma. It is formed by the branching extension of the duct-like structures that radiate from the nipple, finding their way to the extreme confines of the circumference of the organ, surrounded by a delicate investiture of periductal tissue, and by a greater quantity of the interlobular connective tissue. In the male, they end blindly, and in the breasts of men there are no lobules. It may be the same in virgin females. This is contrary to the text-book description which states that the normal female breast at adolescence acquires a lobulated structure.

27

In a recent research upon the histological structure of the normal female breast, based upon material collected from 150 autopsies, it was possible to gather together 35 breasts from women said not to have had children. In a few of these cases misstatements were undoubtedly made by the patients, a few of whose breasts showed undoubted indications of recent lactation, but for the present they are not excluded, and the deductions will be made from the entire group.

Before stating the conclusions, however, it will be well to have some nomenclature by which the classify what was found. For this purpose the following seems sufficient:

1. *Rudimentary Lobules.*—These are vague structures composed of three or four closely approximated ducts surrounded by a minute quantity of periductal tissue, and are widely separated from one another.

2. *Typical Lobules.*—These are shown in all of the textbook pictures, and are composed of collections of alveoli separated by considerable periductal tissue, the whole forming a definite structure, rounded in the sections, and clearly separated from the perilobular connective tissue.

3. *Vestigial Lobules.*—These are found in the breasts of women beyond the menopause, as end results of the process of involution, and atrophy of the parenchyma. They so closely resemble the rudimentary lobules as to make their differentiation difficult and not always possible.

In the 35 cases supposed not to have had children, there were:

Rudimentary lobules	9
Vestigial lobules	9
	18
Typical lobules:	
Small, merging with the rudimentary	9
Full size, and perfect	5
	14
Large lobules suggestive of antecedent lactation	3 3
	35

It is thus seen that of these supposed virgins, one-half had none of the typical text-book lobules in the mammary tissue, but only rudimentary structures, so simple that they might be entirely overlooked as lobules, nine more very small and infrequent lobules, making twenty-seven that lacked the supposed structure of the normal breast as ordinarily taught. Of the remaining eight, three undoubtedly had been pregnant, so that only five of the cases showed the structure supposed to be characteristic of the normal breast.

On the average, therefore, the breast of the young virgin is characterized by a large amount of stroma that is chiefly fibrillar as regards the interlobular tissue, and by a small amount of parenchyma composed of ducts or small groups of ducts forming the rudimentary lobules. The breast of the aged virgin differs through the addition of fat to the interlobular tissue. The breast of the aged virgin with rudimentary lobules may appear identical with that of an aged mother with vestigial lobules.

Lobules were well developed and plentiful in the breasts of all of the 115 women that had borne children.

From what has been said it would seem proper to look upon the lobule of mammary parenchyma as temporary; appearing at a certain time to accomplish a definite purpose, and then disappearing when no longer needed.

The development of the mammary gland evidently depends upon the stimuli that it receives. Under normal conditions these stimuli are general and excite the entire structures uniformy. In the case of the infantile enlargement and secretion there was some doubt whether the cause lay in the maternal blood
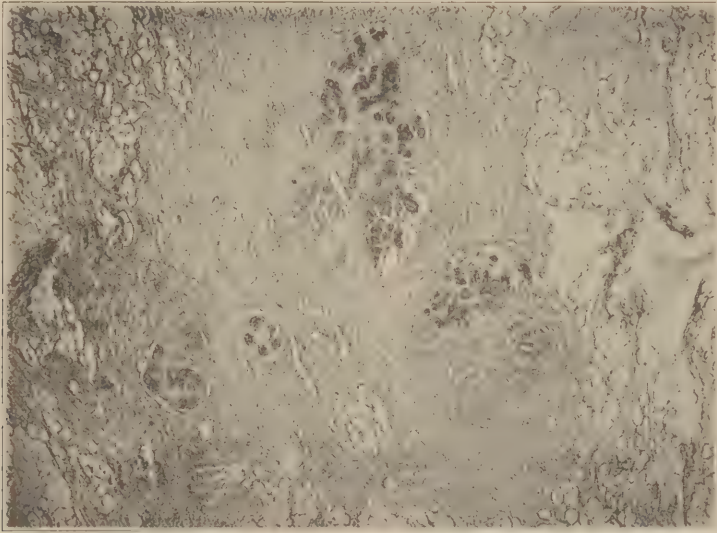
Fig. 286.—Microscopic section of the normal breast of a woman 40 years of age, removed surgically in the Medico-Chirurgical Hospital of Philadelphia, for suspected carcinoma. Typical text-book lobules make up the parenchyma, and there is much fat in the stroma. This is the appearance erroneously supposed to characterize the normal breast, but which only represents its structure at a certain age and condition.

and entered the baby with her milk, or whether it was provoked by external stimuli. In the growth of the breast at adolescence, it undoubtedly lies in the blood of the individual, where it circulates as a hormone. It must be present in both sexes and in varying quantities, as it has been shown that the male breast sometimes develops as only the female should. Its action is sometimes premature, as in the infantile hypertrophy. It sometimes fails in the females, and the breasts remain infantile; on the other hand, it is sometimes present in excess so that the breasts grow to an enormous size and actually become a burden.

Under abnormal conditions they may be local so that circumscribed and small areas of the parenchyma respond. About inflammatory and adenomatous lesions the lobules develop in the virgin breasts.

Through the kindness of Dr. J. C. Bloodgood, we had an opportunity to examine a number of sections of breast tissue adjacent to excised fibro-epithelial tumors. In these cases the patients, virgins, had large and well developed lobules in the breast tissue close to the capsule of the tumors, but smaller and

smaller ones as the distance from the tumors increased. In none of the cases was it possible to know the general structure of the organs, as only the tissue immediately surrounding the tumors had been excised.

But the great and common cause of the development of the breasts is the occurrence of pregnancy. One of its very first signs is swelling and sensitivity of the breasts, soon followed by the presence in the ducts of some moisture, and later by colostrum. But here again the hormone by which the development is initiated and controlled may be absent, so that the breasts fail to develop, or excessive, so that enormous and useless masses of tissue are formed.

FIG. 287.—Virginal or puberty hyper-trophy of the mammae in a patient 14 years of age. The breasts grew so rapidly that in three months they reached to her thighs. (*Malone.*)

FIG. 288.—Pregnancy hypertrophy of the mammary glands in a Chinese woman. (*Latchell.*)

Hypertrophy of the mammary glands must be considered to differ from infantile hypertrophy and gynaecomastia in that it is not the development of a normal gland prematurely or in the wrong sex, but an abnormal growth that surpasses all bounds. With the exception of the non-de-script cases for which no explanation is at hand, it occurs at times when the breasts should normally enlarge i.e., during adolescence or early pregnancy. The normal size having been attained, growth continues, sometimes rapidly, the breasts becoming enormous in two or three months, sometimes slowly, one or two years being required to reach the maximum size.

More than 240 cases are recorded in the literature. Of 182 of these, in which details are given, the hypertrophy affected both breasts uniformly, in 40, one breast only. Of 25 cases said to be unilateral, 8 were on the right, 17 on the left side; in 15 the side was not stated. The growth may be uniform, or may progress by fits and starts, menstruation seeming to accelerate growth.

In a few cases menstruation ceased when the maximum size of the organs was attained. The breasts were largest in Durston's case, where the left, when removed, weighed 64 pounds. The enormous organs are pendulous, reaching to the umbilicus, the pubes, or even to the thighs. The massive organ seems to be attached to the body by a kind of pedicle, beyond which it enlarges to a pyriform structure the weight of which stretches the skin, which usually becomes coarse, so that the nipple flattens.

As the size and weight of the organs usually causes the patient to seek advice with the request that she be disembarrassed of the burden, most cases are treated by amputation. This may, however, not always be necessary, as in nine cases it is said that the breasts became spontaneously smaller, and in a number of cases the amputation of one was followed by the spontaneous diminution of the other. Had nothing been done, both might have diminished in size.

In most cases these hypertrophied organs seem to be incapable of functionating, but in a few there was an abundant secretion of milk. It is also stated that some of the patients nursed their infants, but as the nipples are usually completely flattened, it is difficult to understand how it could have been accomplished.

When a hypertrophied breast is dissected, nothing is found, except what was described by Durston as "extreme bigness." In most cases (especially puberty hypertrophy) the stroma is fibrillar; in some it is fatty. In a few cases it was said to be nodular, but such may have contained tumors as well as been hypertrophic. In no typical case was there any distinct separate mass suggestive of tumor, but some cases of bilateral tumors simulate hypertrophy.

Microscopic examinations usually show structure corresponding with the normal breast, or at least show nothing but breast tissue. It varies according to the age and condition of the patient—i.e., whether she was a virgin, pregnant, or already the mother of children. In most cases (chiefly puberty hypertrophy) the parenchyma seems to have been chiefly composed of duct-like structures, not infrequently dilated and lined with cuboidal epithelium.

In a few cases the patient possessed supernumerary mammary glands, which participated in the hypertrophy—additional proof that it depends upon conditions not local.

In rare cases the enlargement first appeared in the form of a "lump," which increased until the whole breast was affected. This is much like what was pointed out as taking place in some cases of gynecomastia.

The diagnosis of the condition ought to be easy. It differs from tumors in being bilateral, and in being a uniform enlargement; from elephantiasis in that the skin is free from the velvety texture and wrinkling, and of the reported cases of the latter disease, the ages were not those at which hypertrophy is common.

Returning to the point from which digression was made for the purpose of considering the mammary hypertrophy, and remembering that the development of the gland may be dependent upon general or local causes, but that the former are the normal and more frequent ones, and supposing that the particular stimulus acting in the cases under consideration is pregnancy, the evolution of the gland in preparation for lactation progresses, as nearly as can be determined

from the examination of a large number of appropriate specimens, as follows:

Whether there have been only rudimentary lobules, or typical lobules, and whether it be the first or some other pregnancy seems to make but little difference. The glandular tissue proceeds to grow by budding from the ducts, the alveoli, or other epithelial structures with the formation of clusters of new acini —elements comprising the lobules.

We have been able to secure only one case of very early second pregnancy, so feel a little uncertain regarding what happens to the relics of the lobules
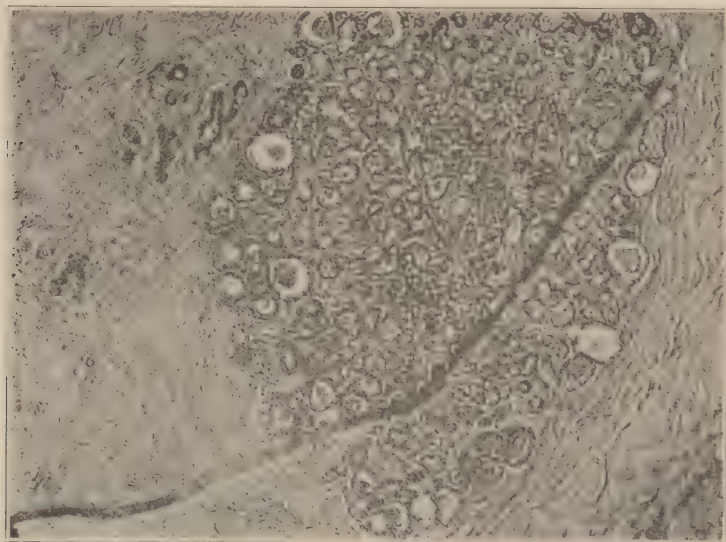
FIG. 289.—Microscopic section of the breast of a colored woman aged 19, who died in the Philadelphia General Hospital of hemorrhage from a ruptured ectopic pregnancy in the third month of her second gestation. The section shows a new lobule developing beside an old one remaining from the previous pregnancy. (?)

remaining from the antecedent lactation. But we found evidence in support of the theory that there may be a separate and new crop of lobules for each successive pregnancy.

In cases as early as the third and fourth months of pregnancy, this budding of the parenchyma is shown by puckering of the ductules of the rudimentary lobules, giving some of them the appearance of having been dilated and collapsed, but looking further over the sections, it soon becomes evident that there are secondary puckers, and also that the cells in the puckers are slightly different in quality from the generality of the cells, being of a slightly darker color, and having slightly larger nuclei. The puckers soon develop into buds solidly filled with cells, and give off secondary solid cellular buds, and these tertiary and quarternary buds and so on, until the little primitive lobule is replaced by a considerable sized mass of glandular parenchyma. As the buds grow, the central cells become vacuolated and disappear, leaving a central lumen about which

the cells are arranged. The periductal tissue increases considerably in quantity, forming a loose fibro-vascular support for the growth of the epithelial elements that soon become so prominent as to eclipse it.

When the primary structure of the breast consists of typical lobules, the periductal tissue first becomes loose and soft, appears to be in excess and myxoid in quality, in some cases. Into this soft tissue the parenchyma then grows by budding.

The size attained by the lobules varies greatly in different cases, and may have something to do with the subsequent ability of the mother to nurse her
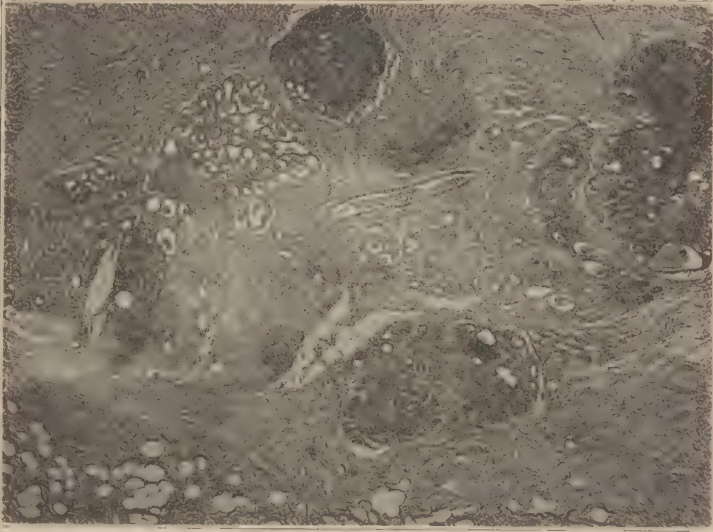
Fig. 290.—Microscopic section of the normal breast of a white woman aged 25 years, who died in the Philadelphia General Hospital during the eighth month of pregnancy. The lobules have already attained to a large size and many of the acini are dilated by beginning secretion, which also fills the ducts. The secretion consists of water containing coagulable protein, but no fats.

baby sufficiently. In some breasts at term there is comparatively little glandular tissue, and although the lobules are large, they are widely separated; in others the lobules are large and numerous. Any adipose tissue contained in the breast disappears, and the growing parenchyma separates the fibres of the connective tissue more and more widely, until it seems to have disappeared.

As had been said, the parenchyma scarcely begins to grow before the buds become canallated by vacuolation of the central cells, and as soon as the lumina are well established, secretion in some form begins. However, it does not begin uniformly, but probably chronologically, the older parts of the new parenchyma first showing signs of secretion. The result is that some of the lumina of the glandular elements gap widely, while others are scarcely perceptible. In the course of twenty-four hours or so after the baby is born, the tissue receives added stimulation, and secretion begins. As lactation continues, it seem probable that the parenchyma continues to increase to meet the requirement of the

growing child. If there is but little parenchyma, and it does not increase, some artificial feeding soon becomes necessary.

After the child has been nursed for some months, the whole breast is usually found to consist of parenchyma with widely dilated lumina, lined with flattened cuboidal cells, each of which contains droplets of fat. All parts of the structure are not uniform; some seem to be active, others resting.

In case the patient aborts, miscarries, has a still birth, or refuses to nurse the child, the breast, at whatever stage of evolution it may have arrived, at once
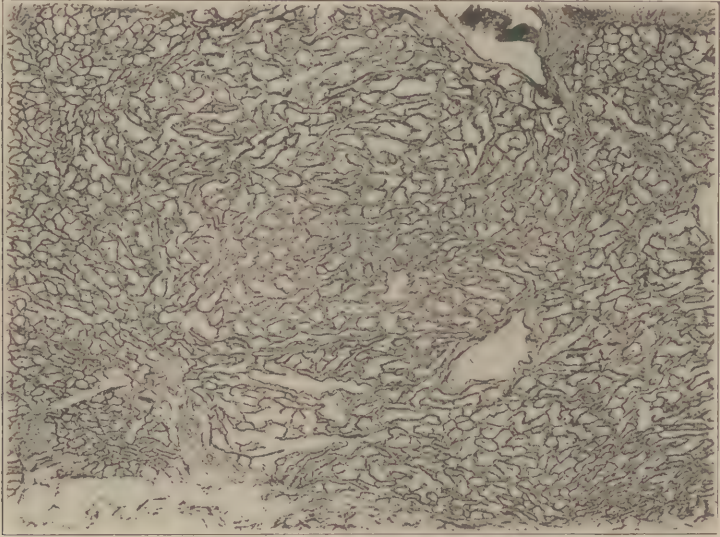
FIG. 291.—Microscopic section showing full lactation hypertrophy. The breast was obtained at an autopsy upon a white woman 34 years of age, mother of six children, the youngest of whom she was nursing at the time of her death in the Philadelphia General Hospital.

begins a structural retrogression, known as *involution*. It must vary in appearance and in degree according to the perfection the breast had achieved at the time it began. Evolution was preparation for expected activity, involution is return to the state of inactivity; the former was characterized by increase of the parenchyma, the latter by its disappearance.

The details of mammary involution are very important because it is subject to certain irregularities which when not understood may be misinterpreted, mistaken for indications of disease, and even confused with tumor growth.

In the ordinary weaning of the child, the quantity of milk becomes less and less sufficient to meet its needs. Other food is then supplied in increasing quantity, until the breast, called upon less and less, is finally withdrawn altogether. But at that time, its activities have not entirely ceased, it is not "dry," and if subjected to microscopic examination, will be found to appear much as at the time of delivery, when the older portions were distended with colostrum, though the newer were empty. Parts are now empty, parts still distended with milky fluid. But this fluid no longer being removed by suction must be

absorbed, and as its water disappears, molecular fat remains to more or less obstruct the ducts. The empty parenchyma collapses, and its small amount of elastic tissue retracts, so that whole lobules, or large parts of lobules, are condensed into an epithelial mass in which gland structure can no longer be defined, as the individual cells soon lose their distinctness, the cytoplasm diminishing rapidly in volume when it no longer contains fatty vacuoles. There then appear densely nucleated tissue areas in a distribution corresponding to the position of the lobules. Into this the surrounding periductal tissue sends growing cells to form fibres, adding to the number and variety of the nuclei, and making it
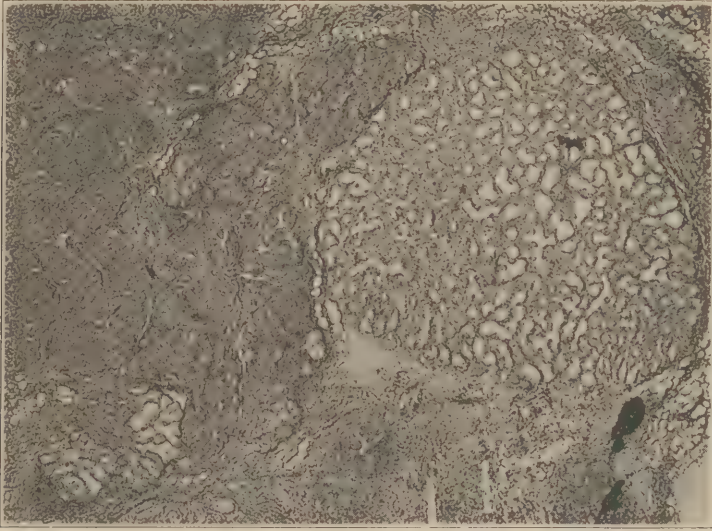
FIG. 292.—Microscopic section of a normal breast obtained at autopsy from a white woman aged 28 years, the mother of four children, all small, but none nursing, who died in the Philadelphia General Hospital. The greater part of the photograph shows a confused cellular mass of collapsed acini undergoing involution, while on the right side is one lobule whose collapse has been delayed and distinctly shows the lactation acini.

more difficult to recognize the nature of individual cells. Little by little the epithelial cells of the acini disappear, leaving the ductules, which are separated by the new growth of periductal tissue, and constitute the alveoli of the lobule that now begins to assume the appearance of the typical text-book lobule. Should the entire breast uniformly undergo such involution, all of its structure would acquire the text-book appearance. But this uniformity seems to be the exception rather than the rule, probably because of the unequal drainage of the tissue, and the obstruction of some of its ducts. The most interesting and important phases of involution have to do with those areas in which retention of secretion tends to prolong involution and modify its results. Yet, as these are, so far as we have been able to determine, but the effects of this mechanical interference, and are to be found more or less widespread in the breasts of most of those whose mammae have reached a stage of development characterized by some phase of secretion, they can scarcely be looked upon as abnormal.

In almost any breast, shortly after lactation, it is possible to find lobules in which about half of the acinar structure has collapsed, while the remainder is open and comparatively unchanged. The epithelial cells of these surviving acini are large, cuboidal, or even cylindrical in shape, and show cytoplasm with an unusual affinity for eosin stain. Their nuclei are sometimes normal in appearance, but more frequently are pale and more uniform in their staining. They may be distinctly abnormal, pale, shrunken and pycnotic, abnormally large, or even enormous in size and irregular in shape, but they remain standing upon the basement membrane of the dilated space to which they belong, seeming to escape the force of the general retrogressive change going on about them.
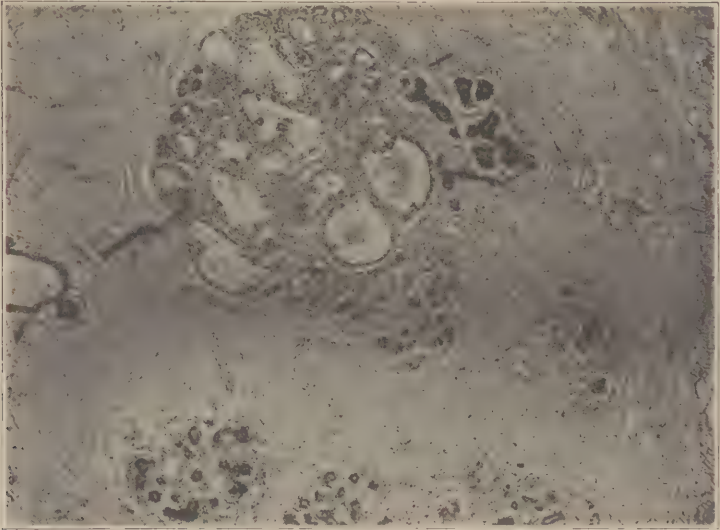
FIG. 293.—Microscopic section showing residual lactation acini in the normal breast of a whitewoman aged 44 years. (*From a case coming to autopsy in the Philadelphia General Hospital.*)

As the rest of the lobule to which they belonged disappears, they seem to accumulate at its periphery, where they occur in groups, looking much like slightly distended ducts. They are usually partly filled with what seems to be a clear jelly, evidently precipitated protein from the retained fluids, or more rarely with granular debris resulting from the involution of neighboring cells. As time goes on these *residual lactation acini* show other changes, of which dilatation is the most important. It does not depend upon secretion, for that is at an end, but presumably upon exudation brought about through the chemical transformation of the retained material.

The exudation and resulting dilatation seem to progress with extreme slowness, so that the residual acini are usually small, but as they dilate, the partition walls between become attenuated and frequently rupture, bringing one after another into a common cavity, into which and from the walls of which the stumps of the former partitions project as simple or slightly branched papillae, covered with the already described and highly characteristic eosinophilic epithe-

lium.   Later, and sometimes very late, such cavities dilate to form cysts varying from visibility to the size of a walnut, or even larger.

Sometimes the small cysts collapse, and then appear as irregular crevices partly filled with an irregular mass of partly degenerated eosinophilic epithelial cells, or amorphus eosinophilic substance resulting from the transformation of the residual cells.

The small cysts thus formed may entirely lose the epithelial lining as the cells seem to be unable to multiply, or may have it only in part.
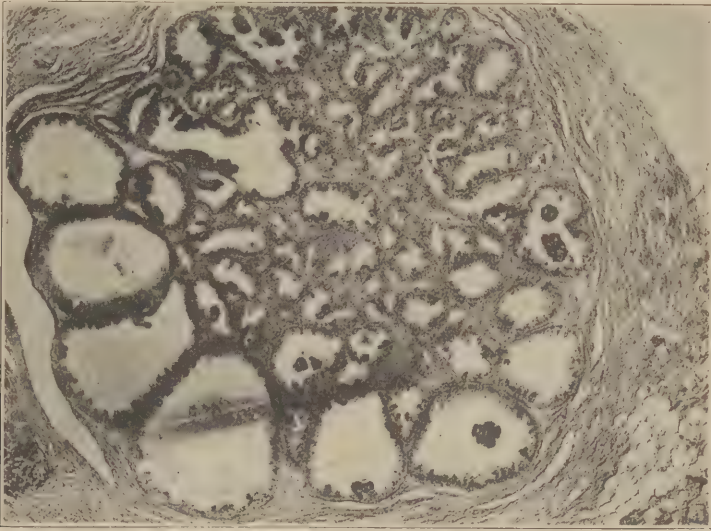
Fig. 294.—Residual lactation acini in the surgically removed breast of a white woman, single, aged 40, whose personal history is not known.   A single area of this kind may mean only that a local stimulation has been followed by evolution comparable to lactation hypertrophy, reached the stage of secretion, and then failed to undergo the customary involution.

The number of cysts thus formed depends upon the number of outlets obstructed, and their size upon the water absorbing affinity of the contents. There may be one or dozens; they may be no larger than a pin-head, or as large as walnuts.

This termination of involution may be regarded as abnormal or otherwise according to the opinion of the reader.   More or less of it occurs in almost every breast that has lactated.   The eosinophilic epithelial lined cysts are to be found in fully 25% of all breasts from women that have lactated, and in nearly every one a few small cysts are present.   But if it becomes so exaggerated as to riddle the breast with large and small cysts, it exceeds the limits of normality, though there is no difference in its nature or origin.

It has, in the past, been looked upon as a disease, and it appears in the literature under many names, of which that used most frequently in this country is *chronic cystic mastitis*.   If it is to be regarded as sufficiently important to have a definite designation, the most appropriate of those in common use seems to be that employed by Warren, "abnormal involution," though we would prefer
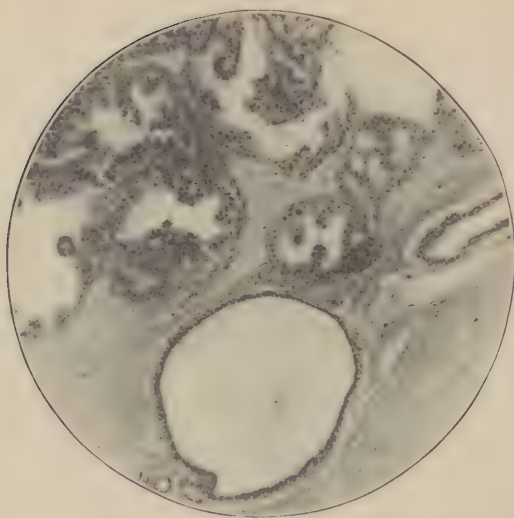
FIG. 295.—Residual lactation acini from a biopsy upon a case suspected to have carcinoma. The breast was removed, but no cancer was found.
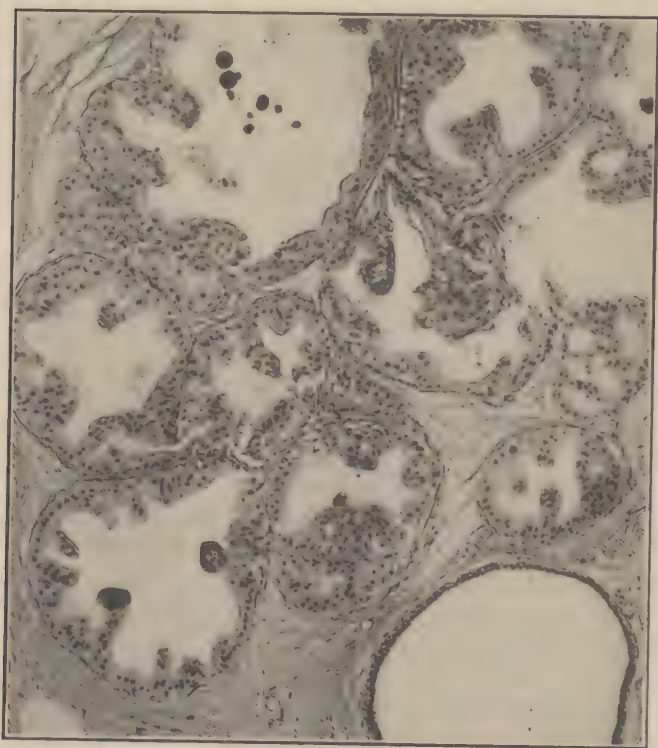
FIG. 296.—Residual lactation acini. Biopsy upon a case of suspected cancer.

to call it *delayed involution*.   Schimmelbush seems to have entirely misunder-
stood its nature, evidently drawing his conclusions from the epithelial lined
spaces and small cysts, with the projecting stumps of the former partitions for
which he could not account.   He looked upon it as a tumor, and called it *cyst-*
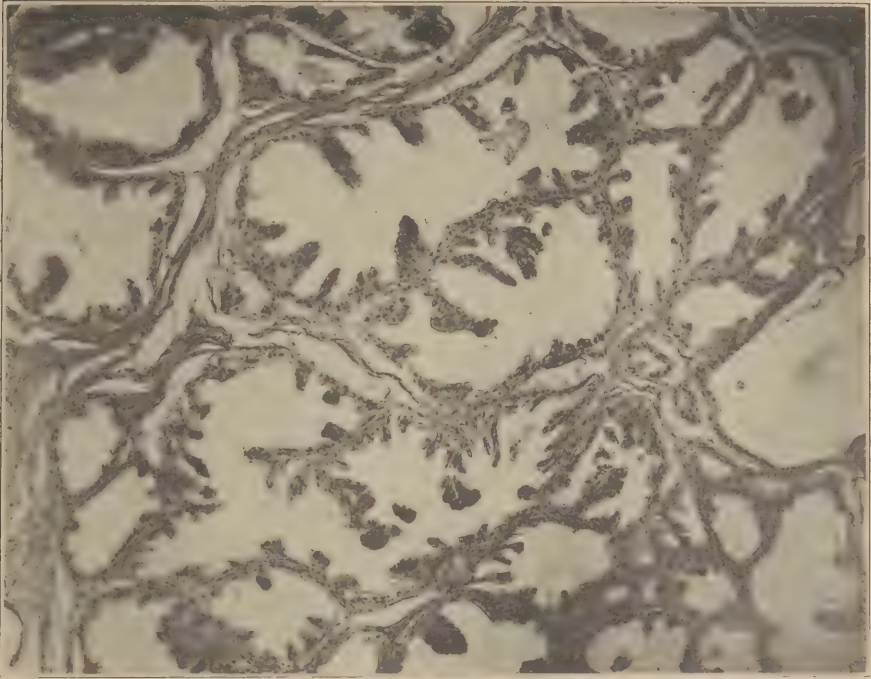
FIG. 297.—Small area of residual full lactation hypertrophy discovered in a breast removed
for a small carcinoma sixteen years after the birth of the patient's youngest child.   (*From a
case operated upon in the Medico-Chirurgical Hospital of Philadelphia.*)

adenoma.   This seems to be a particularly objectionable name, as it tends to
identify a harmless result of involution with a tumor, and has been the source
of the suspicion that it is from these residual lactation acini that cancers develop.
Reclus called the condition *maladie kystique de la mamelle*—cystic disease of
the breast—which would be a very good name if it could be shown that it was a
disease instead of a condition.   But of all the names that most used, chronic
cystic mastitis, is the worst for there is no inflammation, hence no mastitis.

But it may occur to someone that there must be some mistake about this
because residual lactation acini sometimes occur in the breasts of virgins.

In studying such cases as were available it was found that they very rarely
occur except in married women, most of whom had, of course, been pregnant.
There were three sources of material, only one of which could be perfectly
controlled with respect to the virginity of the individuals concerned.   The
collective results are shown in the subjoined table.

TABULATION OF ALL THE CASES IN WHICH RESIDUAL LACTATION ACINI WERE FOUND

I. 150 normal breasts collected at autopsy.
Of these 14 contained residual lactation acini.
Married, 14—100%
Single,   0—0%

II. Breasts surgically removed for chronic cystic mastitis, and not containing cancer.   All
showed the acini.
Married, 53—85%
Single,   8—15%

III. Breasts removed for cancer and found to contain the acini.
Married, 12—91.67%
Single,   1— 8.33%
Total married, 79—89.77%
Total single,   9—10.23%

So, in a general way, the married women with the residual lactation acini
outnumber the single women 10 to 1.   But how is their occurrence in the breasts
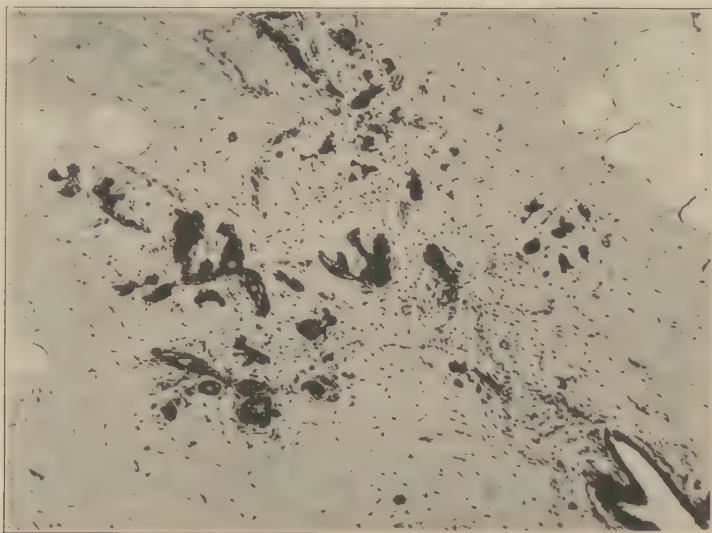
FIG. 298.—Microscopic section of the normal breast of a white woman aged 19 years, who
died in the Philadelphia General Hospital one year after the birth of her baby.   The involu-
tion of the breast has been rapid and so complete that the lobular structure has been dis-
rupted, and only uncircumscribed vestigial remains occur.   The periductal tissue can scarcely
be recognized on account of its confusion with the interlobular connective tissue.

of single women compatible with our theory?   Does it not disprove it?   We
believe not, first because we believe that a number of the unmarried women had
been pregnant.   But there may be other explanations.   It has been shown that
local hypertrophy sometimes goes on in the virgin breast as the result of local
stimulations when fibro-adenomas are present, and it must now be recalled that
secretion of fluid in the virgin breast at the time of menstruation is not uncom-
mon.   In either case it is possible that there are progressions and retrogressions
of the virgin gland.

But the description of the variations of involution would be incomplete were the other element of the lobular structure, the periductal tissue, to be neglected. As soon as the third month of pregnancy, the periductal tissue begins to loosen, soon looks pale and edematous, and thus appears to be present in excessive amount. Later as the parenchyma grows it almost disappears by distribution among the great increase of glandular elements. But when lactation comes to a close, and the epithelial elements begin to disappear through involution, it reappears, and begins to proliferate, and to assume a highly nucleated character, in many cases. What determines this proliferation has not been discovered, but it may have something to do with the transformation products of the disappearing parenchyma. The result varies in different cases.

In some but little new tissue, in others a great excess appears, so that with the disappearance of the epithelium the lobules may give the impression of being enormous in size and fibrotic in structure. The result is not always uniform in the same breast, certain areas show slight increase, others great increase. As the appearance of the excess of the periductal tissue goes hand in hand with the disappearance of the parenchyma, a suspicion has been aroused that the former brings about, or at least facilitates, the latter. Our studies seem to show that the greatest increase of the periductal tissue occurs in youth, and that the involution of the breast occurs most rapidly at that time.

In a few lobules in the breasts of young individuals, the quantity of periductal tissue may become so great as to suggest beginning periductal fibroma. The new tissue also may appear to be dense and firm. But as it is only in young mothers that such appearances are found, and as they do not occur in the breasts of those long surviving the menopause, it seems clear that they are temporary, and not permanent, and probably of no importance. However, they have been misinterpreted, and supposed to be indicative of chronic inflammatory change with fibrosis and another justification for the employment of the name chronic interstitial mastitis.

The study of the 150 normal breasts has shown such variability in the stroma, both as regards the interlobar, interlobular, perilobular and periductal tissues as to make them totally untrustworthy as guides in interpreting the health or disease of the organ except in those cases where they are the seat of such clear signs of disease as may be indicated by inflammatory cellular infiltration, calcification, etc.

If no subsequent pregnancy takes place, indications point in the direction of continued extinction of the mammary lobules, and the gradual return of the tissue to its virginal state—i.e., a state in which the parenchyma consists of tiny vestigial lobules so closely resembling the rudimentary lobules as not to be definitely distinguishable from them, or even to one in which no lobules, but only ducts, can be found.

But involution takes place with differing rapidity in different cases. There are breasts in youth in which every vestige of lactation hypertrophy disappears within a year or two, and there are breasts of older women in which some areas of almost unchanged lactation tissue persist for many years. We have observed

them as long as fifteen years after the last pregnancy. The breasts of elderly women that have had numerous children, and some of them late in life, usually contain numerous lobules, many of them of large size, even as late as the sixth or seventh decades of life.

If a woman whose breast is in process of involution again becomes pregnant the whole series of events starts afresh. New lobules are formed by budding from the remaining parenchyma, and the whole series of changes is repeated.
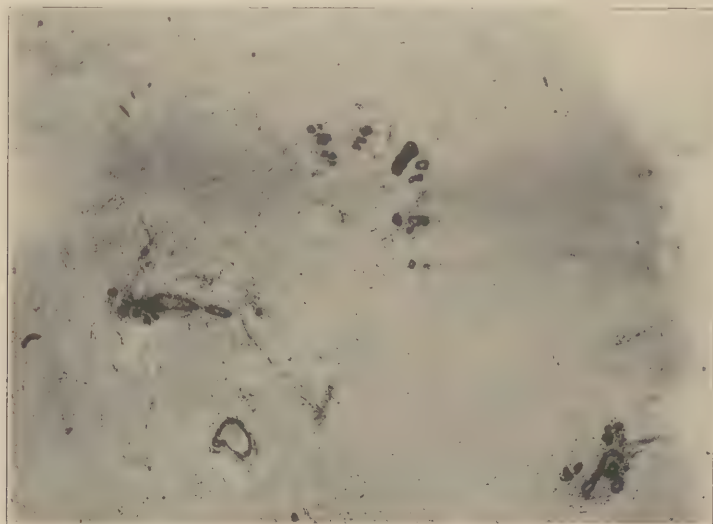
FIG. 299.—Microscopic section of the normal breast of a white woman aged 58 years, who died in the Philadelphia General Hospital. It shows uncircumscribed vestigial lobules such as are common in the post-climacteric breast. The stroma was both fatty, fibrillar and mucinoid.

The more frequently pregnancy, followed by the evolution and involution of the mammary lobules, takes place, the more numerous are the opportunities for the appearance of the irregularities and structural changes incidental upon involution, and the more likely is such a breast to contain the residual lactation acini and the cysts that arise from them.

With the advent of the menopause comes a final disturbance in the physiological activity of the mamma. Some women pass through the period without observing any symptoms calling attention to their breasts, others experience tenderness, slight enlargement, and a small amount of secretion. If both of these conditions are distinct, the patient, knowing that she has reached the cancer age, becomes alarmed, and seeks advice. The breast is then palpated, and its structure is found to be lacking in uniformity and is described as "corded," and sometimes as containing "vague indurations." The anxiety of the patient is then transferred to her doctor who, fearing cancer, sends her to a surgeon, who in turn not infrequently advises amputation of one or both organs. Thus it comes about that many patients are unnecessarily mutilated on account of fear of future evil for which there is no real justification.

Such breasts when examined microscopically nearly always show the irregularities of involution, and both the surgeon and the pathologist content themselves with the thought that as they may be in a "pre-cancerous stage of cancer" the patient is better off for the operation.

Although we have sought for them with great earnestness, no indication that these irregularities of involution lead into cancer has ever been discovered.
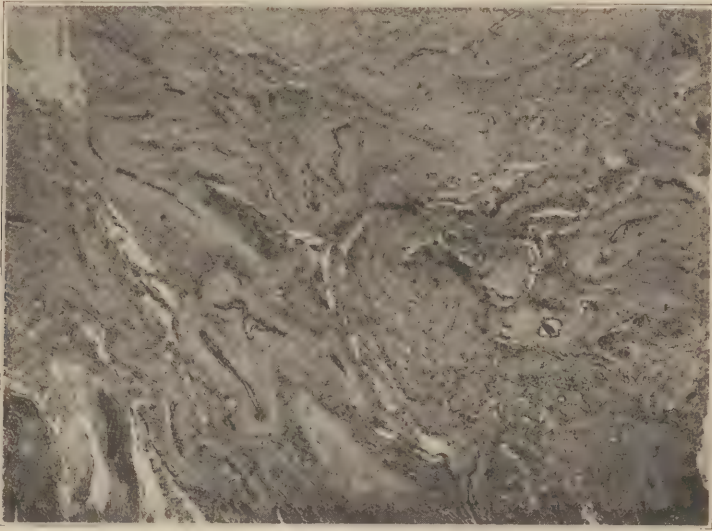
FIG. 300.—Microscopic section of the normal breast of a white woman aged 84 years, a widow, who died in the Philadelphia General Hospital. There are no longer any lobules, but their former position is indicated by epithelial lined fissures surrounded by condensed connective tissue composed of a mixture of periductal and interlobular connective tissue.

As at least 25% of all breasts that have been active contain them in varying degree, their frequent association with cancer is only to be expected. There are many cases of cancer of the breast in which they do not occur. When they do concur, the relation of the two sometimes seems to be very intimate, and cases are not infrequent in which superficial observation leads to the suggestion that it is from them that the cancer has its beginning. But here great caution must be exercised, for the cancer has already begun long since, and has attained to extensive invasion before the operation for its removal. Cancer cells are very prone to grow into whatever spaces the tissue contains, mingling with those of the antecedent structures, and gradually replacing them. The dilatations and small cysts of the delayed involution afford excellent opportunity for this, and into them the cancer cells grow rapidly and more successfully than in the smaller space surrounding them. The result is the deduction that the cancer is springing from these structures, rather than invading them.

Cancer is one of the most terrible and fatal of diseases. The only hope that can be held out to the patient is its complete excision before metastasis has occurred. The profession is very properly endeavoring to educate the public upon the necessity of early and radical treatment.

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But its diagnosis in its earliest stages is difficult, and sometimes impossible, and resolves itself into the surgical treatment of all "lumps in the breast." Many seem to know of no other method of dealing with the situation than the amputation of every breast with a lump or any other suspicious condition in it. Any suggestion of restraint is met with the assertion that "it is best to give the patient the benefit of the doubt."

FIG. 301.—Section of a breast with multiple small involution cysts—chronic cystic mastitis.

The conservative surgeon should endeavor to make an accurate diagnosis, supplementing it with an exploratory operation if necessary, first by the removal of a fragment of tissue under local anaesthesia; second, if necessary, by plastic resection under general anaesthesia. Only by such means can scientific knowledge of the conditions and their future behavior be obtained.

In the preliminary examination certain matters should be taken into consideration that seem to be commonly overlooked. The first of these has to do with the sexual condition of the patient. Is she of the child-bearing age? Is it possible that she is pregnant, and that the disturbance of the breast or breasts is the result of the beginning hypertrophy incidental to that state?

Is she experiencing the mammary disturbance incidental to the menopause?

In either case, great care should be paid to future development, and the patient carefully watched. It recently happened for the second time in our experience that both breasts were removed because of painful enlargement, by a surgeon of broad experience. On the first occasion it turned out that the

patient was pregnant and through the operation was prevented from nourishing her offspring, there being nothing abnormal in the breasts so far as microscopic examination was able to show. On the second, the condition of the patient is not yet known, but the microscopic study of the breasts seems to indicate pregnancy, and reveals nothing abnormal. Such accidents as these should be avoided—in fact they seem to be inexcusable.

The second has to do with the "lumps" the breast may contain. A firm irregular induration so identified with the substance of the mamma as to move with it and not in it, may be cancer, and it may be wise to tell the patient of the probability, and prepare her for a radical operation if necessary. But it would be wise practice to begin by making a plastic resection, exposing the offending area and examining it to make sure. In many cases it will turn out to be a harmless cyst or an area of retarded involution containing several small cysts. In either case, all that need be done is the removal of the induration or cyst.

It is very instructive to see what follows when such treatment is adopted, and for this purpose much can be learned from the experiences of Greenough and Simmons, and Bloodgood. The former simply excised the diseased areas from 83 breasts showing "abnormal involution" but no cancer, when thus exposed, and found that four subsequently developed cancer, thirteen sooner or later showed return of the "abnormal involution," and sixty-two remained well. Four died of intercurrent affections without return of the disease or the development of cancer.

Bloodgood says:

"The educational propaganda is influencing many women to seek immediate advise because of pain, or the palpation of a lump in the breast. I have records of many patients who thought they had felt a lump, or whose physician had thought he had felt a lump, and who on examination by me were found to have no lump (sixty-one cases), or a lump which was one of many indefinite lumps (forty-four cases), or one which was due to simple enlargement of the axillary portion of the breast (twenty-four cases). Here, therefore, we have 129 women who sought advice early because of the educational propaganda, whose breasts on careful palpation presented no indication for operation. It is, therefore, of the greatest importance for all members of the profession who assume the responsibility of diagnosing breast lesions to improve their sense of palpation."

With regard to what is to be done when an actual "lump" is present, he continues:

"The patient is always prepared for complete operation for cancer, and for general anaesthesia. The exploration can be made under procain or gas. One should have on the operating table a medicine glass of pure phenol, one of 95% alcohol, and a third of 50% solution of zinc chloride with swabs. The incision should be made directly over the lump. The moment the operator exposes the tumor and concludes that it is malignant, the exposed area should be swabbed with pure phenol followed by alcohol, the wound packed with a piece of gauze saturated with zinc chloride solution, and closed. Then one should proceed at once with the complete operation for cancer.

"When the operator feels that he must have a frozen section, what shall be the method? Cut out the piece of tumor and wait, or cut out a zone of breast tissue around the tumor and wait? I should favor the latter course, that is, to excise the tumor with a good zone of breast

and temporarily pack the wound with an alcohol sponge.   Up to the present time in my own operations my decision as to the removal of the tumor or the complete operation for cancer has rested on the gross inspection and palpation of the explored lesion, and I have not waited for the frozen section.   Each operator must choose his own method, which should be influenced by the results.

"Among our 350 cases of chronic cystic mastitis, in 210—almost two-thirds—the lesion was a distinct cyst, either with a blue dome, or of the galactocele type.   I hope that my description and illustrations will help operators and pathologists to recognize this type and at least save two-thirds of the patients with chronic cystis mastitis from the unnecessary removal of one or both breasts."

In this extract from his paper upon The Pathology of Chronic Cystic Mastitis of the Female Breast, Nov., 1921, Bloodgood agrees with us that the breast should be conserved and not sacrificed.   He also points out that most of the lumps prove, upon examination, to be harmless cysts.

What is the sensation imparted to the fingers by the tissue of the normal breast, and upon what does it depend?   In youth and virginity it is firm; in age and after frequent lactation it is soft; in both instances it is more or less elastic, and in all cases it is remarkably lacking in uniformity, giving the sensation frequently described as "corded."   The elasticity depends upon the fibrillar and mucinoid quality of the stroma, the softness and flacidity upon the addition of adipose, but the "corded" sensation does not as is sometimes stated depend upon the presence of vessels or ducts, neither does it depend upon the lobulated structure of the organ, but upon its division into lobes and sub-lobes by bands of fibrillar tissue.   It could not depend upon arteries, for they are few, deeply seated and would pulsate, nor upon veins for they are also few and collapsible; it is impossible for it to depend upon the ducts, for they are formed of epithelial cells upon a supporting tissue of extreme thinness; nor could it depend upon the parenchymatous lobules, for they are commonly absent in virginity and as commonly in age, yet in all cases the same general sense of division is imparted to the fingers.

In palpating, allowance must be made for this, and attention paid to nothing but the occasional assymmetrical indurations.   When these are superficial they may be distinctly rounded and more or less movable in the breast tissue, though the cysts arising in the course of involution are commonly surrounded by an area of fibrillar tissue indurated by condensation—by being thrust aside by the growing cyst—and not infrequently approximated to other cysts so as to be immovable.   But when they are deep and the breast large, palpation must give place to inspection.

Cancer is so distinctive in its appearance that it ought to be recognized by the naked eye without difficulty.   The frozen section is not needed. The breast tissue is exposed, and an area of abnormal involution or a cyst is found, which the surgeon leaves or excises as he chooses, and the breast is allowed to remain; or an area of cancer is found, and the breast must be removed.

The frozen section is only apt to be confusing.   It reveals areas of residual lactation tissue, and at once the question is asked, "may this condition not be beginning malignant change?"   "Ought I not remove the breast?"   What help is it?

Cysts of the Breast

From these common single and multiple cysts of the breast that arise in the course of its involution, it seems wise to pass to the consideration of more rare, though no less important, ones. For convenience of description they may be divided as follows:

1. Cysts arising from structures in the skin of the breast.
2. Cysts arising in the parenchyma of the breast.
3. Cysts occurring in the stroma of the breast.
4. Cysts occurring in tumors of the breast.
5. Parasitic cysts of the breast.

1. *Cysts Arising from Structures in the Skin of the Breast.*—Of these the only ones that seem worth mentioning are the *wen*, sebaceous cyst, atheromatous or steatomatous cyst, and the *dermoid*. Upon theoretical grounds there ought to be no difficulty in differentiating these, as the former is acquired, the latter congenital; the former is a retention cyst caused by obstruction of a glandular duct, the latter the result of the sequestration of an ectodermal fragment in the deeper tissues. But practically the differentiation may be impossible. The literature up to 1917 contained references to 37 cysts of the breast that seemed to fall into one or the other of these classes. Nineteen were described as sebaceous cysts, atheromas or steatomas, eighteen as dermoids. In reviewing the case reports it is not always possible to know what kind of a cyst was under discussion. Some of them were considered to be dermoids because hairs were found in their contents, others because of a papillary epithelial layer in the wall. Neither of these counts for much. A few were considered to be dermoids because of their supposed congenital origin, but about that it is difficult to be sure because of the many years that may elapse before such a congenital lesion shows itself. Others were so considered because they seemed to begin as solid formations that later became cystic.

The error seems to lie in misconception of the origin and structure of the sebaceous cyst. It is a mistake to suppose that it results from the simple stoppage of the duct of a sebaceous gland. Those glands are in connection with hair follicles, and if the outlet of such a gland were occluded, the hair follicle would also be obstructed, so that as the former became dilated, the latter would be similarly affected, and the cyst almost inevitably be composed partly of the wall of the sebaceous gland, and partly of the hair follicle. Should the cyst be formed of the sebaceous gland alone, it would be lined with the sebaceous gland cells only and filled with sebum, a condition almost unknown. In almost all cases, sebum forms only a small part of the mushy contents of the cyst, and it may be entirely absent, while the wall almost always consists of stratified squamous epithelium. If the cyst be formed through dilatation of the hair follicle, it would be filled chiefly with lymph to which would be added as much sebum and fatty element as the associated gland would furnish, as well as many squamous cells desquamated from the stratified epithelium of the lining, and such hairs as the root of the follicle would be able to form. A cyst derived as described must always contain the root of at least one hair, and as lanugo hairs

only grow to a short length before being shed, in the course of time the cyst would contain many such, together with that still growing and attached to its root.

If the cyst wall be thin, and its lining relatively simple, and the contents as described, it may be a wen. If it be thick, and contain numerous hair follicles, sebaceous glands and sweat glands, and have well defined papillary layer, it may be a dermoid.

It might be supposed that the position of the cyst would give some indication of its nature, and in some cases it does. For example, if it arise from the skin of the areola near the nipple, where the subjacent muscular tissue causes it to rise into prominence at an early period, it will become the object of solicitude on the part of the patient early, and probably be removed when small and simple, and called a wen. But if it arise beyond the circumference of the areola, the increase in size is followed by sinking into the soft tissue of the breast below rather than by upward projection against the resisting skin. Such cysts may sink for a considerable distance into the mammary tissue. When small the wens are "in the skin," but when they become large, they may seem rather to be attached to it, and then not necessarily derived from it.

Cysts of both varieties grow slowly. They may cause considerable pain, especially when in the male breast, where the tissues are more dense, and correspondingly more difficult to separate and dislocate. They are harmless, and all that is necessary is to remove them. This should be done without opening, if possible, as the smallest portion of the sac remaining may result in recurrence.

Of the 37 cases reported, only three occurred in men. The size of the cysts varied from a cherry-stone to a man's fist. The contents varied, being described as "serum," "fatty matter," "white of egg and cholesterin," "serum containing fatty matter and crystals," "white serous fluid with grumous flakes," "great quantities of epithelium," and "white flaky substance which seemed to be a succession of cuticles, being the same with that which lines it."

With two exceptions the cysts were single and unilocular. One case was said to have been multilocular, and in one case the larger cyst was surrounded by six small ones. All were removed by simple excision, with the exception of one reported by Herrmann which was as large as a man's fist, and in that case the breast was amputated. No case is recorded in which there was subsequent trouble of any kind after the removal of either a sebaceous cyst or a dermoid.

2. *Cysts Arising in the Parenchyma of the Breast.-* Of these it is possible to make several sub-divisions:

(a) Galactocele or lacteal cyst. This results from the accumulation and retention of the normal or modified secretion of the organ, in its larger ducts.

(b) Simple cyst or serous cyst. This results from accumulation of fluids that have nothing to do with secretion, in the ducts.

(c) Cystic disease. This is what has already been described in connection with retarded involution.

(d) Papillary cysts. These are cysts of various origin into which papillary excrescences grow.

Galactoceles are cysts formed by the retention of mammary secretion in obstructed ducts. They are rare, and the literature contains references to

only about 75 cases. They are usually single and unilocular, but if the obstruction be high up, and the ducts connected. it is possible for a multilocular cyst to be formed. They occur in both sexes, but for reasons easily understood are overwhelmingly more common in women than in men. They also occur at all ages, but again for reasons easy to understand are most frequent during that period of life in which the breasts are functional. The youngest case of which there seems to be a record was reported by Cattani, and occurred in a child of 14 months; the oldest was Bouchacourt's case, a woman aged 51 years, unless Velpeau's doubtful case in a man aged 75 years be accepted. The formation of a galactocele may be rapid; Rubesch saw one develop in four days from the time lactation had begun. They may endure for years; Sheild saw one that was 18 years old.

FIG. 302.—Galactocele. (*Rubesch.*)

The general symptomatology of the condition is simple and fairly definite. At some time varying from a few days to several years after the occurrence of lactation (or other secretion), an assymmetrical painless enlargement of one breast is observed. It is usually irregularly rounded, soft, fluctuating, semi-fluctuating, or plastic in consistence, and is free of attachment to the skin above, or to the fascia behind. The suprajacent skin may be marked with enlarged veins as in some of the solid tumors. There are no enlarged axillary lymph-nodes. The size varies from a walnut or a hen's egg to a cocoanut, a man's head, or perhaps even larger. One described by Scarpa was so large and heavy that the breast reached to the thigh of the seated patient, and contained 10 pounds of fluid.

The contents, in different cases, is described as being "thin and milky," "milk," "cream," "buttery," "curdy fluid like white of egg," etc.

The formation of these cysts is sometimes mysterious. It seems quite suffi-cient to say that they result from closure of the lactiferous ducts, but when these are experimentally ligated, no galactocele occurs. However, in each of the cases reported by Jewell, there was an obstruction of the ducts. In one, a lady two weeks after the birth of her second child, complained of pain in one breast, which upon examination was found to have one of the lactiferous ducts of the corresponding lobe of the gland distended and very hard to the touch. The orifice of this duct was found to have become closed by a thin pellicle which formed a bleb. By rupturing that with a needle, creamy fluid could be pressed from the nipple at the duct orifice, the pain ceased and the swelling disap-peared. His other patient, having stopped nursing, applied a breast pump, when "something like a thread" came out of one of the lactiferous ducts of the nipple.

According to the definition here used, the cyst is filled with mammary secretion, and one need only examine a few of the reported cases to see that it is not always milk. That is only to be expected if one stops to consider that milk is only water containing casein, sugar, fat and some salts, in varying proportions. As milk, it has a standard composition, but as mammary secretion it differs at different times. Thus, in infancy, and during pregnancy, it is thin and watery, and contains little fat, being known as colostrum. During the early part of lactation it is rich in fat, but as time passes, the fats gradually diminish, and the milk declines in quality. Galactoceles of early formation may contain fluid analogous to the colostrum; those of later formation, with milk. Supposing the cyst to be filled with milk, can its contents remain unchanged indefinitely? In a few cases they appear to do so; thus, in Scarpa's case, there were 10 pounds of milk, and it must have taken a long time for so much secretion to have collected. But in other cases there seems to be a rapid change. However, one should not be too hasty in concluding that because the contents of a galactocele do not resemble milk, they have undergone great change. Even during the period of its greatest activity, abnormal mammary tissue may not functionate normally, and that part of the gland whose duct is closed can scarcely be regarded as normal. There may, therefore, be abnormalities and disproportions in the component ingredients of the secretion, of which the most frequent seem to be excess of fat or deficiency of water, by which the cyst becomes filled with creamy or buttery material. But the withdrawal of water from the normal secretion might give much the same result. It seems most probable that it is the latter by which the more solid contents are formed. On the other hand, the secretion of the water without the normal addition of fat would explain the watery fluids, and the absorption of watery fluid containing casein, the white of egg material sometimes observed.

The presence of a galactocele is only harmful when it is permitted to remain so long, and become so large that the surrounding mammary tissue is destroyed by atrophy. The condition is benign. All that is necessary is the complete excision of the cyst, which can usually be accomplished without considerable injury to the breast itself. In fresh cases, it might be possible to discover and remove the obstruction, and it may always be well to attempt that before resorting to operation. In cases of large and old cysts, it may be considered good practice to amputate the breast, and thus remove the cyst, but the conservation of the breast should always be practiced where possible.

Simple Cyst or Serous Cyst.—These are much less easy to understand than the galactoceles, for though they arise through the distension of galactiferous ducts, it does not seem to be because they are obstructed, nor are they filled with mammary secretion. Only about two dozen cases could be collected from the literature for analysis. They occur in the breasts of both sexes, at ages varying from infancy to 75 years, the average being 44 years, and they have nothing to do with antecedent lactation or other secretory activity. The cyst in von Dumreicher's case contained 500 c.c of fluid, but most of them are said to be about the size of hens' eggs, and to have had a duration of a "few months."

They usually give rise to no pain or other disturbance, may be discovered accidentally, and form rounded swellings that fluctuate distinctly when superficial, and may be movable in the breast tissue.

They have been observed to fluctuate in size from time to time, and a few have disappeared spontaneously. The dilated duct by which the cyst is formed is not always closed, and in some cases some of the contents have occasionally escaped. If the cyst had been compressed at such a time, the whole contents might have been expressed, though another collection would soon take its place. Attention was called in the chapter upon Cysts to one of these cases pictured by Sheild, with an open duct, through which a bristle was passed.

The contents are variously described as "serous fluid," "clear fluid," "stringy yellow fluid," "reddish fluid," "turbid fluid," and "glairy mucoid fluid."

As there seems to be no reason for supposing that the fluid is secretion, it must be the result of exudation, and take place similarly to the collections that occur in serous spaces, and in the closed vestiges of obsolete embryonal structures. The cause is, however, difficult to find. It seems probable that inflammatory accumulations or infectious agents are the responsible factors.

The cysts are benign. After removal by dissection, they never return. When deeply seated, amputation of the breast has sometime been practiced, but it seems better to perform a plastic resection and dissect out the cyst from behind, returning the organ to its position.

Care must be taken to see that no cancer exists in a breast containing a cyst of any kind. If they coexist, the cancer sometimes grows into the cyst wall, as a dark-colored mass. Bloodgood has described cases of this kind as "cancer cysts," but the term is not well chosen as it tends to confuse the student and make him believe that certain varieties of cysts are malignant, or that certain varieties of cancer are typically cystic. A striking characteristic of cysts occurring in association with cancer is the bloody quality of their contents. Whenever the contents of a cyst are bloody, its wall should be carefully examined for excrescences, and indurations. But even here it should be noted that although the benign serous cysts usually have smooth shining thin walls, they occasionally have them thick and tough, and in very rare cases show a few papillary excrescences. It may be well in operating upon such cases to dissect out with the cyst, a generous portion of the surrounding mammary tissue. But in case such a cyst contains bloody fluid, the breast may be sacrificed.

Papillary Cysts or Papilliferous Cysts; Intracystic Papilloma.—This peculiar and interesting pathological lesion of the breast has received more than a dozen names. As the papilloma seems to be primary and the cyst formed to accommodate it, the name *intra-cystic papilloma* seems most appropriate to us. Terms especially to be avoided are those that carry with them the suggestion that the papilloma is an adenoma, that the condition is malignant, and that it is related to the process of involution. It would be more logical to describe it among the tumors of the breast were it not for the invariable occurrence of the cyst in which the tumor lies, and whose formation regularly accompanies it. It also seems to connect with cysts through resemblance to the papillary excrescences from the walls of certain other cysts, especially those of the ovary.

Two slightly differently appearing though perhaps pathologically entirely different things are included in the descriptions of intra-cystic papilloma. The first, which is certainly the real thing, is a papilloma that grows from the walls of the milk ducts, distending them in order to make a space in which to be accommodated. The second is a papilloma, or several papillomas that grow from the walls of an antecedent cyst, fill and distend it.

The existence of the former is certain, that of the latter questionable.

FIG. 303.—Cyst filled with finger-like papillary excrescences, probably originally an intracanalicular periductal fibroma, but in this advanced stage sometimes called cysto-sarcoma phyllodes. (*From a specimen in the Laboratory of Surgical Pathology of the University of Pennsylvania.*)

The papilloma itself is in no manner different from the soft papillomas that develop from other epithelial covered surfaces, and, so far as is known, may have a similar infectious or inflammatory origin. About that nothing definite is known, except that occasional cases have been said to recover spontaneously, which is true of the surface papilloma.

The tumor is rare, and for analysis only 40 cases could be collected from the literature, and from our collections. Of these 10 were in males, and 30 in females. The average age of the male patients was 48 plus, of the female patients 47 plus, years. The youngest patient was a boy of four years, the oldest a woman aged 81.

The tumor originates without known cause, and although in a few cases preceded by traumatism, there is no reason to suppose that it was of importance, as most of the cases were without such history. It usually affects only one breast, and of the cases reported an equal number occurred in the right and left breasts. In 12 cases the tumor mass is said to have been central in position; in 18 it is spoken of as having been "near the nipple."

In 9 cases in which this relation did not obtain, the greater number occurred in the upper outer quadrant of the breast.

It usually forms an oval or rounded tumor, or elongate rounded swelling situated near the nipple, with the long axes running from it in a radial manner, parallel to the main ducts. In outline it is usually irregular, lobular and lumpy, and rarely forms a single rounded smooth tumor that may be mistaken for a simple or benign cyst. The consistency depends more upon the contents than upon the structure of the wall. It usually gives the examining fingers the impression of a solid tumor, but a feeling of elasticity is present when the cyst contains much fluid.

The tumor is usually well circumscribed, and not attached to the skin or pectoral fascia. It rarely projects beyond the normal level of the mammary skin, and the nipple is usually unchanged, except that in the rare cases in which the tumor has been found to project externally through one of its ducts as a dark reddish mass.

It grows slowly, and never reaches a large size. The ducts not being obstructed in many cases, fluid contents are capable of escaping, and as the cysts enlarge, discharge from the nipple is frequent — occurs in about 75% of the cases. As the tumor is frequently subject to compression and passive hyperemia, the discharge is bloody in about 50% of the cases. This bloody discharge from the nipple in cases with a centrally situated tumor is the most characteristic diagnostic feature. Unfortunately it is not pathognomonic, as there is no discharge in 25% of the cases, and bloody discharge occasionally occurs from other causes.

When the diagnosis is made, either the tumor must be found and removed, or the breast must be amputated. Most surgeons seem to prefer the latter operation, as it is sometimes very difficult to successfully locate the tumor. If the former is chosen, or if the amputated breast is to be examined, one proceeds by making an incision radially from the nipple, down through the areola, to the duct that seems to be distended. Usually the scalpel finds its way into a space, and as it opens, a soft mass, sometimes pinkish gray, sometimes dark red, according to the condition of its circulation, begins to project. It is the papilloma, but its further appearances vary in different cases. Thus, like other papillomas, it may be polypoid, fungoid, arborescent, or dendritic. When the dendrons hang together fairly well, rounded polyps with velvety surfaces spring from the incision; if the villi spread, a dendritic or cauliflower growth is seen. In cases with hyperemia or old hemorrhage, they may be dark, reddish, and be surrounded by reddish or brownish fluid.

There may be one or numerous papillomas growing from the wall of the same duct, and not remote from one another. A papillomatous condition of the duct is sometimes shown by the occurrence of other smaller cysts with smaller papillomas farther down the duct system.

When the papillomas spring from the walls of preformed cysts, their nature is only determinable after removal and opening. The picture is different. There is a well-defined eccentrically situated cyst, from the walls of which and into the interior of which papillomas of various size, and in various numbers, grow, without completely filling it.

These cysts are sometimes multiple, and small, and scattered through the breast. The papilla in them are especially beautiful upon microscopical examination, as they are delicate and fern like in their branchings. Their origin and meaning are not known. These cysts must not be confused with the cysts of delayed involution or "cystic disease" of the breast; they are essentially different, and actively vegetative, the papillomas complexly branched. Those of delayed involution are usually much smaller, and the projecting stumps of the antecedent partitions between the formerly existing acini are very simple —never complexly branched—and are covered with epithelial cells whose cytoplasm lacks its normal granules, and has an abnormal affinity for eosin, while the nuclei, stain homogeneously and lack the reproductive power.

Intracystic papillomas grow slowly as a rule, and rarely attain to a large size. Reported cases are rarely larger than a Tangerine orange. They do not usually cause pain, but may do so. The breast tissue is pushed aside, and may undergo atrophy if the tumor remains long in its substance.

The microscopic appearance is usually characteristic and is beautiful. The complexly branched and divided structure consists of the usual delicate fibrillar and vascular foundation, upon which the epithelial cells are arranged in a single layer, sometimes cuboidal, sometimes columnar in type. If compressed, many of the processes seem to coalesce, and it is probably on account of the approximation and coalescence of the neighboring parts that the structure is frequently mistaken for, or supposed to be related to, adenoma.

The infrequency of the tumor makes it difficult to confirm or refute the different statements regarding its disposition. Greenough and Simmons think that carcinoma supervenes in about 15% of the cases, but Bloodgood places the percentage at 50%.

3. *Cysts Arising in the Stroma of the Breast.*—Of these three require brief mention.

(*a*) Lymphatic cysts. According to case reports published in old writings these are cysts, rarely as large as a hen's egg, frequently multiple, filled with clear fluid, and lined with *endothelium*. When one reflects that in the cysts that occur in mammary involution the epithelial linings, at first columnar, soon become cuboidal, then as they are more and more compressed and stretched become flattened and eventually may disappear altogether, leaving a denuded surface or one lined by endothelium, it seems as though the existence of a true lymphatic cyst was improbable and that it might as well be omitted from future writings.

(*b*) Blood cysts: Hemorrhagic cysts; Hematoma. These are interstitial hemorrhages with subsequent disorganization and colliquation of the infiltrated area, and reactive fibrosis round about to form a wall.

4. *Cysts Occurring in Tumors of the Breast.*—Two kinds of cysts occur in tumors of the breast.

(*a*) Retention and exudation cysts. These occur in tumors of the fibroepithelial group, or as they are frequently called, the adenomas. In all of them there are numerous ducts and acini, lined with epithelium that upon occasion engage in the function of secretion. As these tumors will be considered farther

on, it may be as well to postpone discussion of their secretory activities and the cysts until that time.

(*b*) Colliquation cysts in tumors.   These result from the necrosis, degeneration and colliquation of badly nourished tumor tissue.   In the beginning they are areas of degeneration, then areas of necrosis, more or less sharply separated from the surrounding better nourished substance.   But as time goes on the necrotic tissue, beginning at the center and diminishing towards the periphery, undergoes chemical change with fluidity, which gradually increases until nothing is left but a cavity filled with fluid, bounded by a slimy layer in contact with the surrounding healthy tumor tissue.   In rare cases, in which the tumors continue to grow slowly for months or years, the space may become circumscribed by a layer of endothelium.   Such cysts may occur in myxoma, myxosarcoma, and in different varieties of sarcoma of the breast.

5. *Parasitic Cysts of the Breast.*

(*a*) Echinococcus cysts.   About 50 cases of hydatid or echinococcus cysts of the breasts are recorded in the literature with sufficient accuracy to meet the requirements of correct diagnosis.   With one exception all have occurred in women, and all in adults.   The smallest was as large as a pigeon's egg, the largest the size of a cocoanut.   The shortest time between the discovery of the cyst and that of its observation by a physician, or its treatment, was six months, the longest 21 years.   The cyst is usually discovered by accident, and it is usually erroneously diagnosed simple cyst or benign tumor, on account of its rounded form, slow growth, perfect circumscription and free movability.   Its true nature is only discovered after operative removal.

The diagnosis of the condition is therefore pathological and not clinical. However, it might not be impossible to make a clinical diagnosis if there was reason for supposing echinococcus disease a possibility.

Thus, such cysts not infrequently cause a slight erythema, and occasionally urticaria.   There is usually a high grade eosinophilia.   In some cases the stethoscope placed over the cyst during manipulation permits a sound described as "crepitation" to be heard.   But in no case have these signs been detected in mammary echinococcus disease.   If it were suspected, the content might be withdrawn through a hypodermic needle, and examined for hooklets after centrifugalization.   There might be none, however, in acephalocyst.

After removal, the cyst will vary according to its age and condition.   When small, and sometimes when large, and in the form described as the acephalocyst, it appears as a larger or smaller vesicle filled with clear, colorless, watery fluid, and possessed of a distinctly laminated wall of brittle bluish-white, chitinous material, easily broken into irregular fragments that immediately begin to curl inside out.   This wall, which is the integument of the parasite, is surrounded by a thin sac of connective tissue formed by the host.   When the cyst is larger, and the parasite in active reproduction, it has the same bluish-white homogeneous chitinous wall, but contains a larger or smaller number of daughter vesicles of varying size.   Each of these is, in a certain sense, a diminutive of the parent cyst, but has a thinner and more membranous wall lacking the connective tissue reinforcement, as it is not in contact with the tissues of the host.   The parent

cyst may be so filled with the daughter cysts that they trespass upon one another,
flatten upon the surfaces of contact, and expanding when liberated, give the
impression of occupying more space than was contained in the parent cyst.
They are surrounded by clear limpid fluid. When one of them is opened, it
commonly contains smaller grand-daughter cysts, within which may be others,
and so on. It was calculated by Deve that the number of scolices contained in
one echinococcus cyst might be 400,000 to the cubic centimetre.

Should the parasite die—no cases of dead parasites have been reported as
having been observed in the mamma—the appearances are soon changed by
external suppuration and internal inspissation. In the former case, the para-
sitic nature of the cyst is obscured by the clouding of its contents and the
infiltration of its wall, but if removed, it still may be possible to make a correct
diagnosis. In the latter, the fluid becomes absorbed, the cyst shrinks, and
reactive inflammation with connective tissue proliferation about the wall mask
its nature. The condensed contents sometimes calcify, as may also the sur-
rounding connective tissue. It may then be impossible to do more than con-
jecture as to the probable origin of the curious formation.

In some cases of echinococcus disease the breast was amputated under the
misconception that it contained a tumor.

(b) *Cysticercus Disease of the Breast*.—Two cases of bona fida infestation
of the female breast by Cysticercus cellulosa are on record. In neither was
the diagnosis made. Allessandri amputated the breast of his case supposing
it to be carcinoma, largely basing the opinion upon enlarged lymph-nodes in the
axilla; Guermoprez pricked a small superficial abscess in the breast of his patient,
and found that it contained a small cyst that subsequently sloughed out. Sub-
sequent microscopic examination of the cyst in each revealed a circle of hooklets
and enabled the diagnosis to be made.

TUMORS OF THE MAMMARY GLAND

Cancer

About three-fourths of the tumors of the mammary gland begin in the form of
indefinite, ill-defined indurations, so intimately blended with the substance of
the organ as to move with it, and not to be distinct from it. They are nearly
always painless, may occur in either sex, and at any age, though they are more
than a hundred times more frequent in females than in males, and more than
half of them occur between 40 and 60, the average age being 50 years.
They usually occur in the upper part of the outer hemisphere, and in about half of
the cases, their presence is accompanied by enlargement of the axillary lymph-
nodes of the same side. Nearly all of these prove to be cancers, and it seems,
therefore wise to begin the description of the tumors of the breast with this most
frequent and dangerous variety.

The result of prolonged and careful propaganda of education upon the evils
that result from the neglect of early treatment is a solicitousness that now leads
many women to seek advice because they imagine that "lumps" are present in
their breasts. In the absence of any other cure for cancer than its surgical

eradication, one of the most desirable contributions that could be made to surgery would be a scientific means of determining whether or not "lumps" in the breast were incipient cancer, demanding immediate operation. But thus far no other means of diagnosis has been devised than the inspection of the doubtful tissue, and it seems, therefore, proper to recommend that this be done in all cases.

FIG. 304.—Huge inoperable carcinoma of the breast with axillary and supra-clavicular metastases. (*Deaver and McFarland.*)

The method to be adopted is that used by Bloodgood, and has already been described. There should be very little difficulty in recognizing cancer tissue with the naked eye. We have no figures to prove the statement, but our recollection is that in our examinations of breasts removed in the clinic and sent to the laboratory for study, cancer was never found by microscopic examination where it was not suspected from what the finger and naked eye had found, though occasionally what the eye and finger thought to be cancer was shown by the microscope to be something else. From this it appears that the error is almost always on the side of safety. In some clinics it is the rule to excise fragments of the suspected tissue, and subject them to immediate examination by means of frozen sections. This may be good practice from the point of view of giving the patient the advantage of every assistance that science affords,

but it does not seem to be necessary. The eye and finger of the surgeon ought to be so trained as to recognize cancer.

When the incision is made and the suspected tissue exposed, it may immediately become evident that the suspicious "lump" is a cyst so deeply situated that its nature could not previously be determined. All that is then necessary is to excise it, together with the surrounding indurated breast tissue, except in the very occasional cases in which the contents are bloody, and a papilloma situated in its wall; such are usually associated with malignant disease, and in such cases the breast should be removed.

Or, an area of induration may be exposed, that on section is found to contain a congeries of tiny cysts, closely approximated, and of a size varying from pin heads to small peas. These may be filled with clear fluid, or with yellowish or reddish more or less jelly-like matter. Such an area at once indicates delayed involution, and if no other change in the mammary substance is present, needs no further attention, or, following the practice of Greenough and Simmons, the area may be excised. The condition is benign and harmless. The breast may contain many such areas or may be composed of such tissue so that the excision of the disease is impracticable. It is still, in all probability, harmless and may be neglected, though many prefer to preform a simple amputation.

Occasionally the incision of the suspicious area reveals pus, when it is again clear that there is in all probability no cancer.

But in an overwhelming number of the cases with bona fida "lumps," the knife passes through a dense tissue, sometimes almost cicatricial in character, that is firm and hard to the finger, the cut surface of which is quite different from the shining white of the mammary tissue, in that it is distinctly variegated in color, being made up of minute alternating areas of white, buff, and pink, extending both into the white of the mammary tissue, and the yellow of its neighboring adiposet issue. The white is antecedent mammary gland tissue; the dots of pink, the groups of cancer cells; the buff, groups of degenerated cancer cells and modified fat. Occasional red dots point to minute interstitial hemorrhages, or cut vessels of small size. The whole area has a slightly striated appearance, and may suggest retraction as in a scar. One of our associates always describes it as a "drawn appearance."

All this is perfectly typical of cancer, whether it exist by itself, as it often does, or in association with areas of delayed involution as it occasionally does. When it is present the microscope always shows cancer.

No particular directions are necessary for the microscopic diagnosis of cancer of the breast. It is the same in the breast as in any other organ, and can usually be recognized at a glance. The distinctive features have been so carefully considered in the section upon "Cancer," that it is unnecessary to repeat them here.

But upon looking over the writings upon the subject, it is inevitable that the beginner becomes confused because of attempts to correlate certain conditions with cancer, that probably have nothing to do with cancer, in the hope that thereby the beginning of cancer may be recognized an earlier operation performed, a greater number of lives saved.

The intention is laudable, but unfortunately unfamiliarity with the histology of the normal breast has led to the conclusion that it has a definite standard of structure, variations from which were indicative of malignant change—cancer.

The surprising variety of appearances described in the section upon the involution of the gland prove the futility of endeavoring to lay down rules for judging the beginning of malignant disease through the discovery of such

Fig. 305.—Inoperable encephaloid or medullary carcinoma of the mammary gland.

minute changes as have been pointed out as "primary epithelial hyperplasia," "secondary epithelial hyperplasia," etc. Our studies have made it very doubtful whether the mammary alveoli and acini regularly or even commonly possess a distinct basement membrane, whether the epithelial elements are regularly divided into mammary cells and basket cells, and the "secondary epithelial hyperplasia" is nothing but the result of the confusion that results from the atrophic conditions that form so regular a part of involution after physiological activity.

An examination of many breasts containing small cancers shows that they usually begin at a single focus—rarely from two foci—just as cancer usually begins in one breast, though occasionally in both.

If the surgeon, working in cooperation with the pathologist, bases his statistics upon those cases, only, in which the microscope actually showed cancer to be

present, he will have a very high percentage of returns, and a very small percentage of "cures." But if he includes as cancer all of the cases in which there were involutional irregularities that might be the "beginning" of cancer, he will have a low percentage of returns, and a high percentage of cures. It is partly thus that the statistics of different operating surgeons differ so widely, and that particular operations are made to appear so superior to others.

Experience seems to show that if this test of regarding as cancer only what certainly is cancer be applied, nearly every case suffers from return of the disease, and that if in such cases the axillary lymph-nodes were invaded, it always returns. But the doubtful cases rarely return—probably because most of them were not cancer at all.

In this connection it is wise to remember two things upon which Bloodgood has laid stress. He says, "if you think a condition is cancer, and perform a radical operation, and the disease does not return, how can you ever tell?"

He also says: "It is very interesting to record here again that in breast lesions, when good pathologists disagree as to malignancy, the patient lives; when there is agreement, there is always a large percentage of deaths from cancer." Of course there is. Where they agree there is certainly cancer, for they all know and recognize it; where they disagree, there is no cancer, but some of them are trying to make themselves believe that it exists, though their better judgment tells them it does not, partly in anxiety to give the patient the benefit of every doubt, and partly because of unfamiliarity with certain histological appearances for which they have no satisfactory explanation.

The enlargement of the axillary lymph-nodes, pointed out above as occurring in about half of the cases with "lumps" in the breasts, are of little value in assisting the clinical diagnosis of cancer. They are palpable in only about half of the cases, and their enlargement depends upon causes other than the cancer in about 10% of the cases in which they are present. They occur without cancer in some cases of delayed involution, and in nearly all of the inflammatory and specific inflammatory diseases of the breast.

In cases of cancer, however, it must always be assumed that they are carcinomatous, and no operation should be performed that omits their careful removal.

If the patient does not present herself at the early period that has been under consideration or, having done so, declines operation, the progress of the disease varies according to its type, and according to conditions not easy to understand. In some the disease continues to form a single major mass, that grows slowly with considerable cicatricial contraction, diminishing the size of the breast, and causing retraction of the nipple, minute punctate depressions of the covering skin—pig skin—and only after enduring for a long time, shows metastasis to the lymph nodes. Such cases sometimes live for many years, and die of intercurrent affections. In other cases the axillary nodes enlarge early, and grow to a considerable size, while the primary tumor, confined to one principal node, remains small, or grows also to a large size, forming a soft mass. In still other cases there is a marked tendency to early local dissemination, so that the breast, the sub-jacent muscle, and the surrounding fatty tissue becomes

studded with nodules, some of which may even be found far removed from the seat of primary disease, in the skin, or in the other breast. In rare cases there is widespread dissemination throughout the skin, which becomes nodular, brawny and ulcerated—*cancer en cuirass*.

Fig. 306.—Cancer en cuirass. (*During.*)

However the disease progress, there is always a distinct tendency for it to reach the skin which it first invades, then destroys, so that a more or less extensive ulceration is soon formed. This never shows any tendency to repair, but continuously extends, and becomes covered with a slough composed of necrotic cells that putrify and become extremely offensive. The enlarged lymph-nodes follow the same course, so that additional ulcerations occur in their neighborhood, sometimes becoming continuous with the ulceration of the primary tumor. The interruption of the lymphatics of the arm, occasionally bring about edema that causes great and painful swelling, and in rare cases this is associated with thrombosis of the axillary vein by which the disturbance is greatly increased. If further dissemination of the disease does not effect the occurrence of nodes in the lung, or by extension through the diaphragm invade the liver, the patient usually succumbs to infection through the ulcerations, or hemorrhage from the invaded and weakened veins. If the infection become chronic, and the losses of blood are frequent, she falls into a state of depressed

vitality usually spoken of as *cachexia*. But without these external disturbances, and for reasons not clear, cachexia sometimes appears early, and in a few cases so early as to assist in making the diagnosis before the symptoms are definite.

If the patient be operated upon, the disease may not reappear for many years. Surgeons have attempted to arrive at some conclusion as to the number of years that must pass before the patient shall be considered "cured." This has from time to time been extended, but experience shows that there is no time at which cancer may not return. Indeed the pursuit of this inquiry has resulted only in gloom as to the surgical cure of cancer. The knife does not cure the disease, except in a very small number of cases; that which it does is to postpone its final termination, and modify the train of events. Operation and repeated operation prevent the development of many of the great sloughing masses formerly occurring in the disease, and tend to prevent death from infection and external hemorrhage, giving time for the less obvious and less painful invasion and destruction of internal organs by which life is ended.

Statistics as to the comparative malignancy and benignancy of the different varieties of mammary carcinoma are of little value partly because of the uncertainty of the nomenclature employed by different authors. But it seems to be the consensus of opinion that the more rare varieties are the less fatal. The gelatinous or mucinoid variety is generally regarded as most benign, and after it the adeno-carcinoma, especially its rare form known as the "comedo-carcinoma," or the large acinar adeno-carcinoma. It is also generally conceded that the medullary variety is the most rapidly fatal.

A peculiar variety of columnar-cell carcinoma of the breast occurs in its central part, with or without antecedent intra-cystic papilloma, seeming to arises from tissues belonging to the larger ducts. It is on this account frequently spoken of, especially by English writers, as "duct carcinoma."

Squamous cell carcinoma of the skin of the breast very rarely occurs, springing from the nipple or areola in most cases. It has nothing to do with Paget's disease, though frequently confused with it. Paget's disease, probably has nothing definite to do with carcinoma, and will be considered together with the diseases of the nipple and areola.

Adenoma

The remaining fourth of the tumors of the mammary gland, are entirely different, and are composed, for the most part, of distinctly circumscribed, definitely outlined, more or less freely moveable rounded bodies that mostly occur in the breasts of women averaging 32 years of age (this age is the average of statistics from five different sources), 75% of whom have not borne children, and 95% of whom have not reached the menopause. Very rarely similar tumors occur in the mammae of men.

With the exception of a few cysts, and fewer tumors to be mentioned below, these are usually recognized without difficulty as members of the class of adenomas, and described as *fibro-adenomas*. Some authorities, among whom is Warren, look upon the fibrillar tissue with which they abound, as being the

more important and characteristic element, and accordingly name the tumors *periductal fibroma.*

In many cases these tumors are first observed as minute pea-sized rounded bodies, in the breast of adolescence; rarely they are discovered during childhood; they may first come under observation in mature age. In any case it is impossible to say when they began, for when discovered, they have already attained to a size that permits discovery, and discovery usually being accidental, they may have existed for years. They usually grow very slowly, and sometimes years are required for them to reach the size of an almond.

They are usually without pain or sensation, but are occasionally sensitive and in rare cases cause pain. This is not a sign of malignant disposition; the dangerous tumors are painless in the beginning, and sometimes remain so for a long time.

When they become large enough to attract the patient's attention, and when the doctor is consulted, the tumors are usually about as large as a pigeon's egg, or a plum, and most of them are properly removed because of the general uncertainty as to what mammary tumors of any kind may prove to be, or will eventually do. Occasionally a supposed solid tumor turns out to be a cyst. The tumor appears to the naked eye as a rounded, occasionally slightly lobulated node, that readily permits itself to be enucleated—indeed it is frequently said to "pop out" of the incision. The freedom with which it can be removed varies a good deal, however, and some, being surrounded on all sizes with a perfect capsule, are readily enucleated by the finger, others, seemingly only partly encapsulated, require some additional cutting. But the greater part of the tumor is always free, and there is never any difficulty in determining where it ends. It is said to be best always to remove a part of the breast tissue together with the tumor at that point where it is "adherent to the gland tissue," and Bloodgood has never seen one of the tumors recur when that was done.

When such an excised tumor is divided with a knife, and its cut surface examined, it is found to have a fairly uniform grayish pink color, and consistence. Sometimes it is soft and almost gelatinous.

When subjected to microscopic examination, gross diagnosis is found to be wrong in a few cases. Instead of being glandular in structure, a few prove to be simple, and in very rare cases composed solely of fibrillar connective tissue, or of mucoid tissue, and in a greater number of cases—though these are usually recognized with the naked eye—of adipose tissue. Thus it is evident that there may be occasional fibromas, myxomas and lipomas in the breast, whose occurrence in nodular form causes confusion in making the diagnosis. But they are very rare in comparison, and some caution must be sounded against too hastily concluding that because of the difference in the stroma and scarcity of demonstrable parenchyma, they are entirely different from the adenomas. This will become more clear as the tumors are further considered.

It is sometimes said that the adenomas consist of glandular tissue like that of the mamma. That is a mistake. They do consist of glandular tissue, but it is almost never like that of the gland proper. The latter is made up of a number of definitely arranged connective tissues, in which the parenchyma is distributed

according to a definite plan. The fibro-adenoma is made up of only one—the periductal connective tissue hence the validity of Warren's name, periductal fibroma. This tissue may be of the usual delicate fibrillar appearance, or it may be more loose and edematous, or mucinoid. In it the parenchyma distributes, in the form of ducts which branch and ramify, sometimes sparingly, sometimes plentifully, so that there is no standard quantity of glandular element.

There are no lobules in the tumor, even when the breast surrounding the tumor shows large and well formed lobules. The ducts are simple in structure

FIG. 307.—Adeno-fibroma of the mamma. The tumor is on the left, breast tissue in lactation hypertrophy on the right of the mid-line of the illustration. The separation between the two is distinct; the parenchymatous structures do not blend.

consisting of a layer of cuboidal epithelial cells upon a scarcely demonstrable basement membrane. Demonstration of two layers of cells basket and mammary cells usually fails. The arrangement of the cells is not always regular; sometimes there are superfluous cells that fill the lumina of the ducts. In nearly all cases the ducts are lumenated, and sometimes they gape rather widely. The greater the number of cells in the ducts, the greater is the difficulty of ascribing them to their precise limits; in a few cases they seem to be partly squeezed out of the ducts into the surrounding stroma. This is sometimes interpreted as "beginning malignancy," but seems to be only a part of the general irregularity of structure. There is sometimes much more parenchyma in one part of the tumor than in others, and its arrangement in one part may differ from that in others.

The tumors are pretty well surrounded by encapsulating connective tissue, which is of the perilobular type, and through which the few blood-vessels enter. It is where the vessels enter that the tumor seems to be "adherent."

It seems to be unusual for the stroma to vary; if fibrillar, it is so throughout, if mucoid, mucoid throughout. There is, however, one perplexing exception to this, and that is in cases in which parts of it are cellular.

At this point it is necessary to pause a moment to mention the remaining surprise that sometimes awaits both the surgeon and pathologist when these
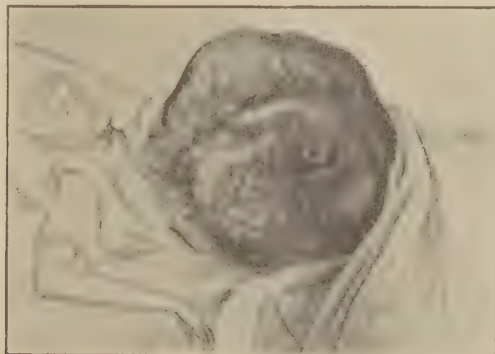
FIG. 308.—Enormous adenoma of the breast. (*Velpeau.*)

little encapsulated tumors are examined microscopically. It is the occasional discovery of one whose stroma is entirely cellular—composed of distinct spindle cells—and therefore indistinguishable from sarcoma. It is important to remember this possibility when consideration is given the possible malignant changes in these tumors.

Fibro-adenomas are not infrequently multiple. There may be several, of different sizes in the same breast, or they may be in both breasts. When one is removed, and subsequently the patient finds another, it may be that the second is as independent of that removed, as though they had both been present at the time of the operation. When multiple, they are not necessarily of precisely the same kind. One may be of the common variety, another of the more rare mucinoid type of stroma. They may also coexist with cysts and with other tumors.

The origin of the fibro-adenoma is uncertain. There seem to be two possibilities: First, the tumor may arise from an embryonal primordium, composed of residual mammary forming substance, which later develops independently, pushes aside the surrounding substance, and thus encapsulates itself.

Or, second, it may result from a purely local hypertrophy of a mammary lobule, at first connected with the gland by its ductules, but later separated from it through attenuation of the ducts by traction. Not until all of the communications are destroyed does the growth become a separate and independent entity. Examination of the margins of some of the tumors shows long, greatly attenuated ductules that seem to be disappearing by atrophy.

When such tumors are removed, that is the end of them in almost all cases. But when they are not removed, interesting things sometimes happens, with which there should be familiarity, lest they be misinterpreted.

In general they keep on growing slowly for a long time, then may stop. It is said that in some cases they retrogress, but there is some doubt about the diagnosis in those cases. They may have been cysts mistaken for tumors.

This slow growth, is however, subject to a surprising change in case the patient becomes pregnant. The tumors, seem to be just as subject to the lactation stimuli as the gland itself, and so soon as the gland begins its pregnancy hypertrophy, the tumor begins to grow. This sometimes excites apprehension, lest the tumor has "changed its type" and is "becoming malignant." But the greatest surprise attaches to the behavior of the tumors when lactation sets in, for, like the gland, the tumor then swells to a greatly enlarged size, becomes tender and sometimes very painful. This is not because anything has happened to the tumor as a tumor, but because it has been stimulated to activity as a gland. The breast is tender and sensitive until it is relieved of part of its contents by the sucking child, but the tumor, having no outlets, and compelled to retain its secretory products, grows and remains large and tender. Sudden enlargement from the size of an almond to that of a walnut or a hen's egg is by no means unusual.

If a fibro-adenoma in such lactation hypertrophy be removed and microscopically examined, its tissue will be found to be different from its quiescent or virginal state. It contains a vastly greater quantity of parenchyma, still consisting essentially of ducts, but now so closely aggregated as to give a highly glandular appearance. In some cases, though there are no lobules, there are so many parenchymatous elements, that the entire structure seems to be composed of acini. Such tumors have been described as "simple adenoma" or as "racemose adenomas," or by some other name implying that they are essentially different from those ordinarily seem.

If the adenoma be permitted to remain, however, it soon ceases to be painful, because secretion ceases, and in the course of time, it grows smaller, especially at the end of lactation. It then undergoes involution, somewhat after the fashion of the breast itself. Thereafter, it never again perfectly resembles its original state, any more than the breast itself does, but always shows a modification of structure by which its previous activity can be recognized.

A few such tumors escape lactation hypertrophy, and then show no subsequent alteration of histological structure.

But if fibro-adenomas are permitted to remain in the breast indefinitely, they sometimes keep on growing, and may attain to a great size. In past generations, when a surgical operation was a formidable matter, some of these tumors grew to exceed the size of the human head, and to weigh many pounds. Such were frequently cystic, and showed many of the areas of retrogressive change common in tumors, among which were calcification of the stroma, hemorrhagic extravasations, large cysts filled with buttery accumulations resulting from the activities associated with antecedent lactations, and occasional cholesteatomatous formations. They sometimes ulcerated externally, but

showed no evidence of malignancy, either by invading neighboring structures, or by metastasis.

When the arrangement of the parenchyma and stroma of the small tumors is studied, it is found possible to divide them into three groups:
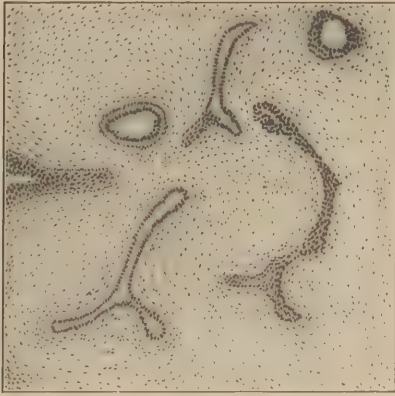
FIG. 309.—Intercanalicular adenofibroma of mamma. The fibroconnective tissue bears no definite relation to the glandular canals.
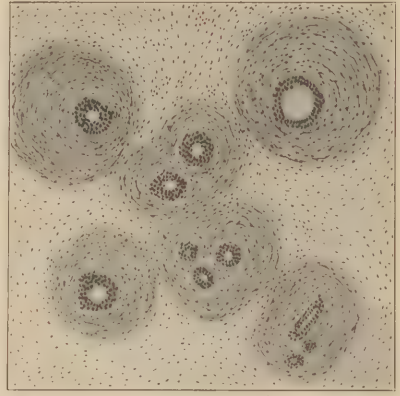
FIG. 310.—Pericanalicular adenofibroma of mamma. The fibroconnective tissue shows a peculiar concentric relation to the glandular canals. This arrangement is rare.

1. Those in which there is no definite arrangement. For these no particular name has been suggested, but they might be called *canalicular* or perhaps still better *inter-canalicular*, in order to keep them separated from the following:

2. Those in which the periductal tissue is arranged about the ducts more or less regularly in a concentric manner, *peri-canalicular*, and
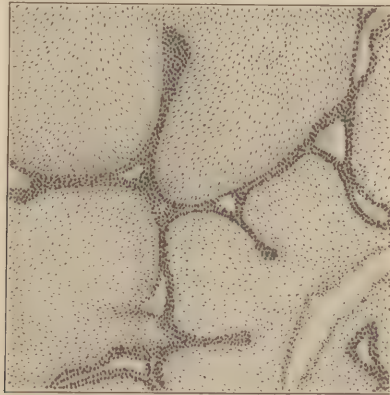
FIG. 311.—Intracanalicular adenofibroma of mamma. Papillary connective-tissue growths project into the glandular canals. This is the most frequent arrangement.

3. Those in which the connective tissue seems to grow into the ducts, dilating distorting and distending them by polypoid rounded masses—*intra-canalicular*.

These different varieties are of pathological interest only; it is not known why the differences occur, or what they mean. From the clinical point of view

they mean nothing at present. But they do have a certain significance in connection with a tumor formerly much written about, but fortunately neglected at present, the *cysto-sarcoma phyllodes*. What our predecessors knew by this name seems to have been large intra-canalicular periductal fibromas into the dilated spaces of which rounded ingrowths of connective tissue grew in finger-like masses, of great size. But the perplexing feature in regard to the name, is the addition of the word sarcoma. How did that arise?

An inconsiderable number of supposed adenomatous tumors, sometimes grow very slowly for many years, than take on a more and more rapid growth, until they attain to a large size, and metastasis to other organs brings about the death of the patient. Microscopic examination of these tumors shows the structure of sarcoma.

It is quite possible that some of these large tumors described by the earlier writers, behaved clinically like sarcoma, and that some examined with the microscope had stroma sufficiently cellular to be regarded as sarcoma, hence the name cysto-sarcoma phyllodes.

We are thus brought to the last of the exceptions to the rule that the rounded moveable nodular tumors occurring in the breasts of comparatively young women are fibro-adenomas; some are sarcomas.

Sarcoma of the Mammary Gland

About 3% of mammary tumors are classified as sarcomas. As the number of cases occurring in the experience of any one individual is usually too small to enable him to discuss the subject with authority, the proper approach seemed to be through an analysis of the cases recorded in the literature, and for that purpose, we made, in 1917, a careful review of the whole subject, succeeding in assembling a total of 838 cases. But the results obtained from the analysis of this large series was less satisfactory than might have been expected, because of the careless method of reporting many of the cases, and the uncertainty of many of the diagnoses.

Sarcoma of the breast may occur at any age from infancy to the century mark, but the greatest number of cases come under observation between the 30th and 50th years. It may occur in either sex, but is more than 30 times more frequent in women than in men. It has already been pointed out that sarcoma is one of those tumors seeming to be influenced in growth by trauma, but in the breast trauma seems more frequently to result in the development of carcinoma, except in women of advanced years. There is a curious reversal of the usual rule with reference to malignancy. The earlier a cancer appears, the more malignant it is apt to be, but the later a sarcoma appears, the less malignant it is apt to be.

Warren divided mammary sarcomas into two groups:

1. *Non-indigenous sarcoma*, arising from tissues not essentially parts of the mammary gland—i.e., the connective tissue of the gland.

2. *Indigenous sarcoma*, arising from an essential tissue of the gland—the periductal tissue.

The non-indigenous sarcomas are extremely rare, and are among those found to occur after injury. The indigenous sarcomas are the common variety,

and may be further described as *complicating sarcomas*, in that they appear in such manner as to suggest that they arise through transformation in the stroma of fibro-adenomas.

The greater number of mammary sarcomas are not recognized until having been operatively removed as fibro-adenomas, they were subjected to microscopic examination.

The clinical appearance and course of the two tumors is the same in nearly all cases. The tumor is first recognized as a small rounded, movable nodule in the breast. It is painless, grows very slowly, and causes no apprehension.

It is supposed to be a fibro-adenoma, and perhaps is removed as such, and both the pathologist and surgeon are surprised when the microscope reveals a stroma composed almost entirely of spindle cells. The parenchyma may be absent, or present in very small quantity only, or appear as usual in fibro-adenomas. Such a tumor may never be heard from again, when there may be some suspicion that the tumor was not sarcoma after all, but merely a fibro-adenoma with unusually cellular stroma.

But supposing it is not removed. It may then grow, very slowly, for years, attracting little attention and causing no trouble, until suddenly it is observed to be larger, then to grow rapidly, until in a few months it increases ten or twenty fold. It is then usually supposed to have changed its type of structure, and become transformed from a benign to a malignant tumor.

It may, of course, have done so, but its behavior is not inconsistent with primitive malignant structure, and delayed malignant manifestation. One only needs recall the behavior of the mixed tumor of the parotid to remember the possibility of a tumor destined to become malignant, growing slowly and occasioning no injury for many years, then beginning rapid and destructive tendencies and a fatal termination, to realize that.

The analysis of the cases shows that there are three types of development; (1) that in which the tumor remaining small and growing very slowly for a long time suddenly takes on rapid development; (2) that in which a small nodule appears and rapidly grows to a large size; (3) and that in which the small nodule very gradually and regularly grows until after a number of years it becomes a large tumor.

In the beginning they all appear alike, in the end they appear much alike; the difference lies only in the regularity and rapidity of growth.

As these tumors become larger, they usually become nodular, and not infrequently develop soft, and sometimes fluctuating areas that may be recognized as cysts. When such are present, it has been customary to describe them as *cysto-sarcomas*, but that need not imply any essential difference in the structure.

The growth displaces the surrounding breast tissue, and as the size increases, the tumor gradually finds its way to the surface. At that time, it is definitely circumscribed, and freely movable, but as the skin marked by large veins, becomes stretched over it, atrophy followed by infection and inflammation, sets in, and it slowly becomes attached to the tumor, and finally destroyed, so that considerable sized ulcerations, through the deeper of which the capsule of

the tumor may be visible, are formed.   As more and more of the skin becomes
destroyed, the tumor begins to project, and if the capsule be destroyed by ulcer-
ation, or if it be traumatically injured, its substance may fungate as a large
soft bleeding necrotic offensive mass.   There is no enlargement of the axillary
lymph-nodes except as may occur in consequence of the infection, and there
are no disturbances of the general health, nor any metastases.

At this time the tumor may be removed, still under the diagnosis of fibro-
adenoma containing cysts.   Such a tumor even though the microscope may

FIG. 312.—Sarcoma complicating a huge intra-canalicular myxoma of the breast.   (*Bloodgood*.)

show sarcomatous structure of its stroma may not return, but about that it is
difficult to be sure, because of the fact that the greater number of available
case reports stop with the removal of the tumor, and its gross and microscopic
examination.

But in many cases we are informed that within a year or so, the tumor does
return, usually in the scar, and another operation is required, and then later
another, and perhaps another.   The persistence with which these tumors may
return is emphasized by the experiences of various surgeons. S. D. Gross
operated 22 times, Bryant 5 times, Hoffman 12 times, Riedel 8 times, Erichsen
6 times, Heath 6 times, Gay 6 times, Billroth 4 times, and Howard 4 times,
each upon a single patient, in attempting to prolong life and finally extirpate
the disease.   The prolonged period during which the disease remains local, in
contrast with so many other varieties of sarcoma, is shown by the fact that the
patient upon whom Gross operated 22 times for the removal of 51 recurrent
tumors, during a period of four years, afterward remained alive and well for
ten years and nine months without either return or metastasis.

But this is not true in all cases, and in some metastasis occurs fairly early,
and destroys the patient.   In general, however, metastasis is much less com-
mon in the indigenous complicating varieties of sarcoma, than in the more rare
non-indigenous sarcomas.

The development of the sarcoma from the antecedent peri-ductal fibroma is
supposed to be indicated by the following:

1. The tumors having existed in the breast for a long time, take on a rapidity of growth out of all proportion to what has gone before, without pregnancy or lactation to explain it.

2. The tumors are always distinctly encapsulated.

3. They are nearly always described as adeno-sarcomas, adeno-cystic sarcomas, etc.

But the rare non-indigenous sarcomas are different; they are not so distinctly encapsulated, they do not remain latent for years before taking on the rapid growth, and they are without any parenchyma of the breast in their histological make-up.

They also far more frequently return after excision, and are usually early metastatic and fatal.

The number of varieties of sarcoma that appears in the literature is surprising; we have found the following:—

Spindle cell sarcoma..	206
Round cell sarcoma..	90
Giant cell sarcoma..	28
Mixed and irregular cell sarcoma..................................	14
Melanotic sarcoma..	23
Myxo-sarcoma...	27
Angio-sarcoma (plexiform, endothelioma and perithelioma)...........	23
Adeno-sarcoma (not cystic).......................................	24
Adeno-sarcoma (cystic)—Cysto-sarcoma.............................	169
Chondro-sarcoma and osteo-sarcoma................................	31
Cholesteatomas—all cysto-sarcomas...............................	23
Alveolar sarcomas..	3
Lympho-sarcoma—including leukemic tumors, etc....................	10
Chloroma...	3
Sarco-carcinoma..	21
Non-de-script..	143
	838

The first seven of these may be accepted as giving the actual varieties of sarcoma that occur in the mammary gland. The remainder are either lesions not correctly classed as sarcomas, or fall into one of the other groups.

If we exclude the non-de-script sarcomas from the calculation because it is not stated by the reporter of those cases what the microscopic structure of the tumors was, if we also exclude the chloromas and leukemic tumors as not being sarcomas, if we conclude that in all probability the so-called alveolar sarcomas were really carcinomas, and if we then add to the 206 spindle cell tumors, the mixed cell tumors, the giant cell tumors, the adeno-sarcomas and cyst-adeno sarcomas, chondro and osteo-sarcomas, nearly all of which are likely to be chiefly composed of spindle cells, it will be found that the mammary sarcomas chiefly composed of spindle cells outnumber those chiefly composed of round cells just about 5:1.

In at least one case it was found that a mammary sarcoma contained striated muscle tissue (Billroth). Remembering that the stroma of an adenoma, though usually composed of periductal fibrillar tissue, is commonly mucoid, and that in

such tumors cartilage and bone not infrequently occur, the finding of an occasional tumor in which there is striated muscle, only seems one step in the direction that indicates that these tumors are in reality not simple, but mixed tumors. It is true that the mucoid tissue might be the result of degeneration, but it will be remembered that when the subject of myxoma was under dis-

FIG. 313.—Periductal, complicating sarcoma of the breast. (*Deaver and McFarland.*)

cussion, it was pointed out that there is no such tissue in the adult body, and that the continuous production of mucus as the cells increase, is characteristic of the embryonal mucous tissue, from which the tumor probably descends. It might be supposed that the presence of cartilage and even of bone might be referable to anaplasia followed by metaplasia, and Marchand would support that view, but when it comes to the presence of the striated muscle cells, where are they to come from? What too is to be regarded as the probable source of the giant cells of the giant cell variety of the tumor? They are of the typical bone marrow variety, yet how can they be supposed to gain admission to the breast?

Although at one time it seemed to us that the theory of metaplasia was sufficient to explain all of these occurrences, we have gradually been led to adopt a different view, and now think the evidence points more strongly in the direction of the composit and complicated tumors being "mixed" and resulting from the inclusion in the developing breast of some elements from the sclerotomes and myotomes of the developing wall of the thorax. In this we are glad to find ourselves in accord with Lecene.

The large cystic sarcomas are interestingly complex formations. The stroma may be partly fibrillar, partly mucoid, partly chondrous, partly osseous, partly cellular. It may be only in certain areas that there are enough cells to justify the diagnosis sarcoma. In this matrix the parenchyma has developed

as usual, then become cystically distended through the collection of materials resulting from secretion or exudation. In most cases these can be attributed to activities initiated by antecedent pregnancies but sometimes they seem to be the result of local stimulations in the tumor itself. The retained secretion undergoes alterations with the passage of time, and as the secretion is usually primarily milky, it secondarily becomes creamy or buttery, or composed of masses of fatty acids and cholesterin, as in those cases called cholesteatomas. Additional modifications may result through the occurrence of hemorrhage or suppuration into the cyst contents. These cysts are at first lined by columnar or cuboidal epithelium, rarely by squamous epithelium. If the latter is present, it may be accounted for through metaplasia, but seems more probably to be the result of the inclusion of ectodermal material, and another evidence in favor of the tumor being mixed. Some of the cysts may be without linings, the cells having become extinguished through the pressure and chemical alterations. In addition, other cysts may develop as the result of degeneration and colliquation of the stroma. These have no linings, and are usually ill-defined and bounded by necrotic tissue.

Mixed tumors of the parotid evince their malignancy through excessive and invasive growth of the epithelial elements, and become carcinomas; but in the breast, the carcinomatous development of an adenomatous tumor is one of the rarest events, and there are almost no cases in which such supposed change having been found upon microscopic examination, it was confirmed by the subsequent clinical behavior of the tumor.

Of the non-indigenous sarcomas strange things are sometimes reported. Thus of the round cell variety, a certain number have been observed to give metastatis to the axillary lymph-nodes. This is not strictly incompatible with the behavior of sarcoma, but is more like carcinoma and in reflecting upon it one is reminded that there are cases in which the microscopic differentiation between sarcoma and carcinoma is made difficult because of the small size of the carcinoma cells, which aggregate in masses with little infiltra-

Fig. 314. —Section of a breast containing a well circumscribed sarcoma adjacent to a carcinoma. (*Kennedy and Caes.*)

tion of the surrounding tissue. Diagnosis of sarcoma would undoubtedly be made if only a single block of tissue, or a single slide should be available for examination.

Most of the melanotic sarcomas develop from moles of the skin, but some arise in the deeper tissues, probably from distributed chromatophores to which mention was made in the discussion of pigmented tumors (q.v.). These tumors are, as usual, intensely malignant, and early metastatic.

An interesting variation is found in tumors that are carcinomas so far as the invasive growth of their epithelial cells is concerned, and sarcomatous so far as the cellular character of the stroma is concerned. In a few the carcinomatous
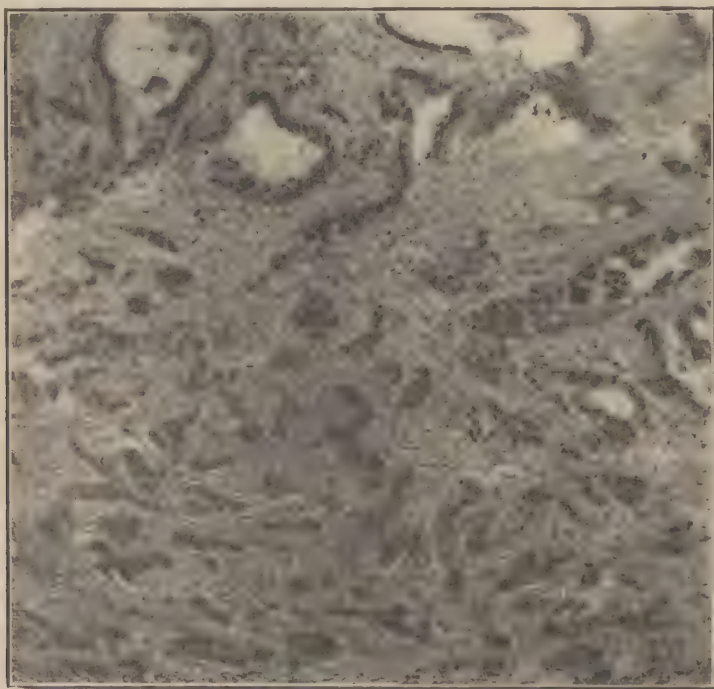
FIG. 315.—Microscopic appearance of the carcinoma in the breast shown in Fig. 314.

elements were metastatic to the axillary lymph-nodes as definite carcinoma, while the sarcomatous elements were metastatic to other parts of the body to which they were carried by the blood, and were definitely sarcomas. Such tumors are sometimes called "mixed tumors," sometimes sarco-carcinoma, sometimes carcino-sarcoma. Such behavior is not inconsistent with that of "mixed tumors."

An interesting case of doubly malignant mammary tumor was reported by Kennedy and Case, and consisted of a typical and unmistakable carcinoma, at one edge of which, in contact with the carcinoma tissue, but not invaded by it, was an equally unmistakable rounded, well circumscribed but non-encapsulated sarcoma. The latter was about the size of a walnut, homogeneous in texture, almost white in color, and composed entirely of spindle cells. It was very probably an non-indigenous sarcoma.

The prognosis of mammary sarcoma is made difficult through lack of clinical information. As is so commonly the case with published surgical reports of

tumors, most of them end either with the report of the operation, or the micro-scopic diagnosis that followed it; rarely does the operator think it worth while to delay publication until he knows the future history of the patient.   It may also probably occur to the reader that many of the diagnoses are pathological and not clinical.   Are all of the cases microscopically diagnosed sarcoma because of excessively cellular stroma really sarcoma?   What really is sarcoma?   A clini-cal or pathological entity?

Gross concluded that the prognosis in mammary sarcoma was far better than in carcinoma, the average duration of life in the former being seven years,

FIG. 316.—Sarcomatous tumor—the separate rounded tumor—of the carcinomatous breast shown in Fig. 314.

as contrasted with the latter, in which it was only 37 months.   He also regarded the probability of cure as far greater, 13.8% of his sarcoma cases having been cured by operation, while only 10.4% of his carcinoma cases were.

The non-indigenous sarcomas appear to be much more rapid in growth, and correspondingly more malignant than the indigenous variety, but this may be rather an opinion than a fact, because of the difficulty of determining which cases are non-indigenous tumors.

In carcinoma it is of the utmost importance not to delay operation because of the certainty that secondaries will soon develop.   In sarcoma, however, metastasis comes very late; tumors of cocoanut size are usually still local, and can be removed as easily as smaller ones.

The treatment of sarcoma is no longer purely surgical in the sense of depend-ing upon operation alone.   Many cases have recovered after the injection of Coley's mixed toxines of streptococcus and bacillus prodigiosus, and a much greater number after treatment by the X-rays and radium.

30

Miscellaneous Tumors of the Breast

Fibroma, if the peri-ductal variety be excluded, is one of the most rare of the mammary tumors. Indeed, it is a question whether real fibromas exist, or whether the new growths described as such were not fibromatoids. Virchow described three varieties of mammary fibroma:

1. Fibroma diffusum, characterized by the formation of hard connective tissue in the stroma of the gland, the glandular elements becoming contracted, obstructed and dilated, or remaining unaltered.
2. Fibroma tuberosum, in which circumscribed hard nodules, were supposed to form as a result of interstitial mastitis, glandular tissue occasionally being caught in the connective tissue.
3. Fibroma intercanaliculare papillare, undoubtedly the peri-ductal fibroma or fibroadenoma of the present nomenclature.

To these Nordmann thinks a fourth should be added:

4. Fibroma plexiforme. The only case of this variety seems to have been a tumor observed by himself, in which newly-formed connective tissue followed and surrounded the ducts in a plexiform manner.

With the exception of the third variety, it is very doubtful whether any will bear the test of careful scrutiny for admission to the tumor class.

Lipoma is occasionally seen. Zesas has divided them into the following:

1. Intra-glandular lipomas—those with which we are really concerned.
   - I. Unilateral.
   - II. Bilateral and symmetrical.
2. Extra-glandular lipomas { Retro-mammary. / Subcutaneous.

Unilateral intra-mammary lipomas are rare, but have been observed in both sexes. When small they are sometimes mistaken for cysts. The few that contain glandular elements, should be excluded from the class, and placed among the fibro-adenomas with fatty stroma, as probable "mixed tumors."

Large lipoma sometimes attain to a great size. One reported by Atkins weighed 25 pounds.

Bilateral symmetrical lipomas occur in both sexes. They may also attain a large size, and in the case of a Kaffir girl aged 12 years, reported by Hoenigsberger, were so large as to make the breasts resemble those of puberty hypertrophy, as the organs were symmetrically enlarged to an extent that caused them to hang down to the pubes. It is a pity that his report gives so little detail, as one is left in doubt as to whether the case was not, after all, the adipose variety of puberty hypertrophy.

Occasionally lipomas are multiple in the same breast. Under these circumstances they do not necessarily all make their appearance at the same time. It may be that the rare cases of recurrent lipomas of the breast, were but successively appearing multiple lipomas, having nothing to do with one another, and not necessarily malignant. A few cases, in which the fatty tissue was partly myxoid, were recurrent and sarcomatous.

Myxomas are rare. They are described as rounded, encapsulated soft, grayish juicy tumors, easily removed, and occasionally inclined to return.

In considering them, one must remember that the myxoid periductal fibromas are sometimes called "myxomas," without further designation.

Chondroma and **Osteoma** of the breast are rare tumors of which only about a dozen cases have been reported. Some of these may have been fibro-adenomas in the stroma of which these specialized varieties of connective tissue developed. But cases have been reported as simple chondroma and osteoma, so the possibility of such uncomplicated occurrence must be admitted. Both begin as nodes, and grow slowly, usually for years before attaining to a considerable size. The chondroma is hard and firm, the osteoma hard and stony. To which class the tumor belonged was rarely determined before its removal.

They are always well encapsulated, and as has already been pointed out, are probably congenital, and the result of the inclusion in the tissue of the breast of some of the cells of the sclerotomes of the developing embryonal chest wall.

Angiomas. Only about seven cases of intra-mammary angiomas have been reported. Cutaneous angiomas occurring upon the breast and in the nipple are excluded from the present consideration.

Two varieties of intra-mammary angioma are described; the circumscribed, the diffuse.

I. *Circumscribed Angioma.*—This is remarkable in that the mass of newly-formed blood-vessels is surrounded and isolated by a membrane similar to the capsule of a benign tumor, or if not thus encapsulated, is so well circumscribed that the whole bundle of vessels remains close together.

II. *Diffuse Angioma.*—In this variety the vascular new formation is distributed throughout the breast increasing its size, and giving it a bluish color, proportionate to the number of vessels close to the surface. The tumor may be centrally situated, the vessels radiating more or less distinctly from the nipple, or may be excentric, and occupy some quadrant of the gland. It can rarely be definitely located; it is not painful, it is usually easily compressible, at once regaining its size when the pressure is relieved. The vessels may be small, or some of them as large as the finger. Mammary angiomas may pulsate.

Nearly all of the patients were young, but a few were of mature years. It is not usually possible to determine how long the tumors have existed. They may develop with the gland and remain undiscovered, until growth, discoloration, the sense of pulsation, or, as in the case reported by Asmus, the blood mixed with the secreted milk attracts attention.

Some of the angiomas were small, others as large as a mandarin orange; in a few cases the whole breast was considerably increased in size.

In the case of deeply imbedded angiomas the diagnosis is sometimes difficult to make, and some cases were mistaken for carcinoma, others for adenomas.

In some cases the tumor was excised, in others the breast was amputated. There is always probability of hemorrhage and the case reported by Image, Hake and Liston died of hemorrhage the evening of the operation.

In some cases mammary angiomas have recurred. They were probably angio-sarcomas, as were also the few cases that are said to have become metastatic.

THE INFECTIOUS DISEASES OF THE BREAST

I. Acute Infection

There are three periods at which the mammary tissue seems to be particularly prone to suffer from infection, all of which correspond to its periods of physiological activity, viz., that of infantile secretion, that of adolescent development, and that of lactation. Three types of inflammatory disturbance are therefore described:

> Mastitis neonatorum.
> Mastitis adolescentium.
> Mastitis puerperium.

In each of these periods the breast becomes hyperemic, enlarges and secretes, and in each of them there is, temporarily, at least, communication between the skin on the outside, and the ducts on the inside, at a time when the latter contain that upon which bacteria entering from the skin may thrive and vegetate.

1. *Mastitis Neonatorum.*—This term is sometimes loosely applied to the normal enlargement, sensitiveness and secretion of the infantile breast to which reference was made at considerable length in describing the normal evolution of the mammary glands of both sexes. That is not mastitis, and should not be so called unless to the usual phenomena are added definite signs of inflammation, and especially suppuration. This unfortunately occasionally follows meddlesome interference on the part of ignorant care takers who think it necessary to express the secretion from the babies' breasts. When the breasts actually inflame, they swell far more than usual, become red in color, and are very painful, so that the baby cries when they are touched, and has fever.

2. *Mastitis Adolescentium.*—In regard to this affection, the same care must be taken to exclude the normal hyperemia and tenderness, with its attendant secretion, from the pathological condition of inflammation. In the temporary enlargement of the evolving mammae of both sexes there is not, as a rule, and there should not be any real inflammation. When it does occur, it is the result of accident, medlesomeness, or lack of resisting power.

It is said that in girls, it precedes the actual development of the breast and that after it has subsided, the organ again returns to its juvenile size, to grow later. But, however that may be, in either sex, the occurrence of inflammation is characterized by an unusual degree of pain, throbbing, and painful swelling of first one organ, and then of the other, should the trouble be bilateral. In a few cases there is a discharge of blood from the nipple. The condition usually resolves, and the occurrence of suppuration is very rare. The usual duration is not longer than a week. Suppuration is preceded by an induration that gradually softens and becomes boggy.

3. *Mastitis Puerperium.*—This is the most frequent and by far the most important variety of inflammation of the mammary gland. It seems to occur in about 1% of lactating women, with equal frequency in both breasts, being most common during the first lactation, and diminishing in frequency with each additional lactation. However, it does not follow that if a patient have escaped the trouble at the first or second lactation, she is immune. It may

occur after any lactation or in each of several lactations. It usually is unilateral, but may be bilateral, the breasts being affected simultaneously or successively. Different writers give different estimates of its bilateral occurrence, some placing it at 15%, others as high as 30%. It may be superficial and subcutaneous, local and circumscribed, or it may be diffuse, phlegmonous, gangrenous, and very fatal.

The means by which the infectious agents reach the tissues is not definitely known, but the following channels are to be considered:

1. *The Infection May be Local and Endogenous.*—In these cases it may be supposed to result from the admission to the deeper tissues, of the bacteria already in the milk ducts.

2. *The Infection May be Local but Exogenous.*—Here, as the result of chaps and fissures of the nipple, bacteria from the clothing, or from the mouth of the baby, may be admitted to the lymphatics, and so find their way to the deeper tissues of the breast. These are probably by far the most frequent cases.

3. *The Infection is Generalized and Hematogenous.*—This variety is most frequent in cases of puerperal infection. But it may occur in either sex independently of lactation, and occasion inflammation and abscess formation during or after certain infectious diseases, notably scarlet fever, where gangrenous mastitis sometimes occurs.

But, taking the common puerperal variety as the type affection, it is found to occur most frequently either at the beginning or at the end of lactation. In 57 cases studied by Nunn, the time of occurrence was found to be

First month	19
Second month	14
Third month	2
Fourth month	1
Sixth month	2
Seventh month	0
Eighth month	1
Ninth month	1
Tenth month	17
	—
	57

The periods at the beginning and ending of nursing are, therefore, those attended with the greatest danger. This may be because of the chapped nipples at the beginning, and the baby's teeth at the end. But, the stagnation of the milk in the breast of the mother of the weaned child is supposed to be an important factor. That this brings about histological alterations of the breast tissue, has already been described; now it is seen to afford an opportunity for bacteria to multiply and effect infection.

Acute mastitis unfortunately usually results in suppuration. Mammary abscesses may be:

    I. Subcutaneous

    II. Intra-mammary

    III. Retro-mammary

I. Subcutaneous Mammary Abscess.—This is not common. It occurs in cases in which there has been infection of the superficial lymphatics through fissured nipples. The area of inflammation is adjacent to the areola, and usually is soon followed by bulging of the surface tissues, spontaneous rupture and

evacuation if not operatively relieved. These abscesses rarely burrow into the deeper tissue of the breast. They are painful, but are not dangerous, and occasion very little constitutional disturbance.

II. Intra-mammary Abscess.—This is the common variety, and occurs in two sub varieties:

      1. The circumscribed type,
      2. The diffuse type.

1. *Circumscribed Intra-mammary Abscess.*—Here, following hyperemia, the breast swells, becomes very painful, and shows a dusky red discoloration of its skin. The patient sufferes from pain and fever. The abscess develops slowly, and if the infection occurs at several foci, they tend to coalesce. In quite a number of cases, the local symptoms are so slight that the true nature of the disturbance is overlooked until the abscess is well developed.

2. *Diffuse Intra-mammary Abscess.*—This differs from the former in that the inflammation tends to spread throughout the entire breast, transforming it into a series of communicating pus cavities. The progress of this disease in its worst forms diffuse phlegmon—is so rapid as occasionally to cause the breast to become gangrenous in a few hours, or the infection becomes generalized so rapidly that patients have died in 48 hours.

III. *Retro-mammary Abscess.*—This is almost without exception the result of the extension of the infection and suppuration from the gland itself, the retromammary space, with the formation of a second and communicating abscess cavity. With its occurrence, the breast, already enlarged, becomes much larger, and is pushed forward. At the same time the patient begins to show signs of increased constitutional disturbance—sepsis, with hectic temperature, chills, sweats, coated tongue, and prostration. Examination of the breast itself shows less local involvement than would be expected with such impressive general symptoms. Here care must be taken not to be misled into supposing that the whole train of symptoms is the result of exceptionally virulent bacteria.

Whatever other measures may be used to prepare for it or to supplement it, the only treatment for mammary abscess is incision, evacuation and free drainage. How this is to be done is not in the province of the pathologist to say. But the earlier this treatment be instituted, the more thorough it is, and the more freely the breast tissue is drained, the more rapid and complete the recovery. These statements apply just as appropriately to those rare forms of purulent mastitis occurring apart from the puerperium, in the course of typhoid fever, scarlet fever, or after typhoid fever, as to the puerperal cases, and to the still more rare cases that affect the male breast as well as to those occurring in the female.

The recovery from purulent mastitis is naturally followed by a variable amount of cicatrization, and deformity. There should be no confusion of this condition with the so-called chronic sclerosing mastitis, about which more will be said shortly.

But not all of the pyogenic infections of the breast pursue the simple course described. In a few, the extent of the infection, and of the following suppura-

tion is so limited that it escapes observation, and is not subjected to operation. A deeply situated small abscess may then remain concealed and the infectious agents perhaps remain alive for years in the substance of the breast long after all signs of inflammation have subsided. Under these circumstances different things may happen. Should the patient again become pregnant, and the local conditions change accordingly, a large purulent infiltration of the breast may occur, and a large abscess form. But if that does not happen, gradual absorption of the pus, associated with cicatrization, may result in the formation of a firm induration easily mistaken for a tumor, though in the course of time it resorbs. Or, long afterwards the pus, slowly burrowing may reach the surface and evacuate, leaving a sinus slow to heal on account of the indurated and infiltrated tissue that has formed about it. If the treatment of the abscess has been attempted in a half hearted manner, and insufficient incision and drainage afforded, healing may take place, and later be followed by residual abscess, requiring renewed incision and drainage, or manifest itself through the appearance of a new and small abscess in the cicatrix, that opens and leaves a sinus slow to heal.

In a few cases, in which unusual micro-organisms are present, the mammary abscess, though apparently sufficiently opened, and properly drained, fails to heal kindly, but continues to discharge for an indefinite time.

Occasional mammary abscesses occur independently of any of the causes thus far mentioned, and to them a brief reference must be made. They may result (1), from direct infection as the result of traumatic injuries of the breast, with external opening; (2), from traumatic injury without external opening; (3), from the extension to the breast of infectious agents from subjacent carious ribs, etc.; (4), from metastatic distribution and secondary, colonization of micro-organisms in the breast in cases of generalized infection.

All of these are rare, and usually sufficiently evident to need no further comment, and the treatment and results resemble those of the ordinary lactation abscess, except when they result from the presence of tubercle bacilli.

Whenever chronic abscesses or chronic sinuses develop in the mamma, tuberculosis, or some other specific granulomatous disease should always be suspected and looked for. Before considering them, however, it will be necessary to refer to a peculiar condition described under the name "*chronic interstitial mastitis.*" It seems doubtful whether this is a definite entity. Some cases are nothing but cicatrization following repair after suppuration or other destruction of parts of the breast; some, as those described by Billroth, in which the entire breast becomes transformed into a small hard shrivelled mass of dense scar tissue, may have been cases of unrecognized "withering scirrhus." Certainly such cases are not to be distinguished clinically from carcinoma.

But the term has appealed to some pathologists as appropriate for cases in which they fancied that the breast contained an excess of fibrillar tissue. All such cases that have come under our observation were normal breasts. The supposition that the fibrillar tissue had increased at the expense of the parenchyma, being a mistaken deduction based upon lack of acquaintance with the variation in structure manifested by the normal organs at different periods

of life and activity, or unfamiliarity with the variations incidental to involution.

We have not yet seen any case to which the term "chronic interstitial mastitis" could be applied with justification.

Still more perplexing are those cases of disturbance of the male breast to which the same term is applied by some, and to which others have referred as "chronic hypertrophic mastitis," "chronic indurative mastitis," "chronic induration," "diffuse interstitial mastitis," and "chronic sclerosing mastitis."

Some of these are said to be the result of antecedent infection, when they obviously do not constitute a definite entity, but cicatrization following repair of the injured tissue. But others are without such antecedent history. A few are said to follow traumatism without infection or suppuration, and most of the cases occur without any explanation.

The condition makes its appearance at any time between the 18th and 50th years, the average age being 26 years. In 31 cases recorded in the literature, the right breast was affected 17 times, the left 10 times, both 4 times.

The symptoms are pain and tumor. The pain is sometimes very slight—tenderness rather than actual pain. The tumor sometimes consists of hard nodules situated in the center of the organ below the nipple, and among the larger ducts. In the course of time these may increase and coalesce, until the whole breast is affected, and presents an appearance like that of a young female organ, with enlargement and some pigmentation of the nipple. Remembering what was said of the condition known as gynecomastia, it will at once be seen that there is no essential difference. To all appearances the local or general disturbances given as causes of the trouble, acted as stimulants followed by physiological reaction in the form of the temporary or permanent assumption of the female type of mammary development. The occurrence of nodules is without significance, as in cases of which we have knowledge, nodular formations, at first supposed to be tumors occurred, later coalesced to form a general enlargement of the breast, and finally the whole thing subsided, and the organ returned to its usual size and appearance. The nodules that form under these circumstances are never circumscribed, and therefore arouse apprehension that they may be cancer. It is on this account that they are so commonly removed, and no cancer being found, some other name has to be applied to them, and as all that is usually found upon microscopical examination, is a dense fibrillar stroma—which is normal to the male breast in youth—and a varying quantity of parenchyma, it is inferred that the condition depends upon increase of the connective tissue, and is, hence, chronic sclerosing mastitis. In this connection let it not be forgotten that the enlargement of the female breast at the time of adolescence does not depend upon the growth of the parenchyma so much as upon that of the fibrillar stroma, and that a number of excellent histologists to whom we showed section of normal breasts of young virgins, immediately made the diagnosis of "chronic interstitial mastitis." There seems, therefore, to be little reason for believing that general or circumscribed, or even tumor-like developments of the male breast, fibrillar in structure, and indefinitely separated

from the surrounding adipose tissue, may not be mammary hypertrophy in response to local or general stimulation.

Osler points out that "A remarkable hypertrophy of the mammary gland may occur in pulmonary tuberculosis, most commonly in males. It may be only on the affected side." He proceeds to add, however, that "it is a chronic interstitial mammitis (Allot)," and that "mastitis adolescentium, not very uncommon, is not necessarily suggestive of pulmonary tuberculosis." Presumably what he mentions is that just under discussion, but we have had no opportunity to study any such cases.

TUBERCULOSIS

Between 1881 and 1914 a total of 90 cases of tuberculosis of the breast were reported in the literature, 10 being in males, and 80 in females. The youngest patient was a girl of 14, the oldest a widow 64 years of age. More than half of the cases occurred between the 20th and 50th years, and more than half of them in married women. 48 cases were primary, 29 secondary, the remainder uncertain.

The first symptom to call attention to the trouble, is a painless lump in the breast, hence the question of cancer must immediately be dealt with. Unfortunately not enough consideration is always given to the differential diagnosis, and many cases have been unnecessarily subjected to radical amputation. The proper way to avoid that accident, is to generally adopt the method of exploring the breast in all cases of doubtful diagnosis before proceeding with the operation for cancer. Should that be done, the respective appearances of the cancerous and tuberculous lesions are sufficiently distinctive to make the differential diagnosis easy.

But, in addition to the lump, there are fistulas in about one-half of the cases when they come under observation. As these are very rare in cancer, they afford additional evidence that the disease is something else, and immediately suggest the appropriateness of additional diagnostic measures such as endeavors to find the tubercle bacilli in the discharges, the employment of tuberculin, etc.

The condition of the lymph-nodes affords little aid for they are found enlarged and tuberculous in about one half of the cases.

The disease assumes any of the following described forms:

1. *Acute Miliary Tuberculous Mastitis.*—This is always secondary, and unimportant from the surgical point of view, being part of general miliary tuberculosis.

2. *Nodular Tuberculous Mastitis.*—The great majority of cases are of the discrete nodular variety. The bacilli lodge in the stroma of the gland, rather than in the duct or periductal tissues and excite localized tubercle formation, with gradual increase in size and the formation of outlying daughter tubercles that amalgamate with the parent lesion until a large, and palpable mass is formed. This varies in size, but rarely exceeds a hen's egg. As a rule it remains unattached to the structures underlying the breast, and does not connect with the skin until late. The mass thus formed is irregular in contour, ill-defined, and apt to be tender. It is of irregular consistence, and some part

usually is soft and may fluctuate. The inflammatory reaction is marked, and the formation of cicatricial tissue usually causes retraction of the nipple, especially if the mass is centrally located. In most cases the skin eventually becomes adherent, commonly at the periphery of the areola, and assumes a dark red color. The lesion points and ruptures spontaneously, permitting the necrotic and purulent contents to evacuate, after which a sinus remains. Later other sinuses form, as the first sometimes heals. Or, the first remains open and the whole lesion becomes surrounded by dense cicatricial tissue studded with miliary tubercles.

3. *Disseminated Nodular Tuberculous Mastitis.*—In this form the disease spreads quickly to numerous subordinate centers, so that the organ becomes more widely diseased. It is said to be more common during lactation. The whole organ may be studded with tuberculous nodules.

4. *Sclerosing Tuberculous Mastitis.*—This is a mammary lesion comparable to fibroid tuberculosis of the lung, in that with a moderate amount of actual tuberculous tissue, there is a maximum of connective tissue formation and cicatrization. Sinuses are of rare occurrence, and the diagnosis is correspondingly difficult. It may be impossible to clinically differentiate it from scirrhus.

5. *Mastitis Tuberculosa Obliterans.*—In this variety the lesions seem chiefly to surround the milk ducts, destroying the epithelial lining, filling the lumen with the products of tuberculous transformation, and finally obliterating them. In Ingier's case the nipple ulcerated away. Tubercle bacilli were found in the fluid expressed from the cut surface of the mass.

Tuberculosis of the mammary gland is one of the most benign forms of the disease, and no case has died directly from it. In most cases it is sufficient to excise the area affected, and supply drainage. But if the disease has extended widely, it may be necessary to excise the breast. If the axillary nodes are badly diseased, the radical operation may be performed.

<center>SYPHILIS</center>

Syphilis of the breast may be primary, secondary or tertiary, but is rare in all stages.

1. *The Primary Lesion or Chancre.*—This always occurs in the region of the nipple and areola, and is the result of the application of a mouth in which there are mucous patches, to nipples that are abraded, fissured, or traumatically injured. The usual cause is the application of a congenitally syphilitic infant to the breast of a wet nurse. Such chancres, usually unilateral, may be bilateral. They may manifest all of the usual characteristics of the Hunterian chancre, or may lack most of them, and sometimes appear only as minute erosions or fissures at the base of the nipple, that might lack all suspicion were it not for the fact that they are entirely painless, whereas fissured nipples are notoriously painful. Chancres of this region are also apt to be multiple, and Gravagna has called attention to a specimen in the St. Louis Hospital in Paris, that shows 28 separate chancres about the nipples of a wet-nurse infected by a syphilitic infant. These chancres may be extremely large, and Petges has reported one 10 cm. in diameter centered about the nipple. It was red, had clean borders,

secreted abundant lymph, and was covered with exuberant granulations that projected for nearly 2 cm. The axillary lymph-nodes were enlarged and hard. The nipple and areola were lost in the lesion, the true nature of which was made certain only when the secondary roseola appeared.

In other cases the chancre was incrusted, forming a well circumscribed rounded ulceration surmounted by a tightly adhering brown or dirty gray scab, the removal of which revealed the Hunterian chancre.

Mammary chancres may become phagedenic, destroying more or less of the mammary tissue, leading to the loss of the nipple, and through erosion, may lead to the occurrence of milk fistulas.

II. *The Secondary Lesions.*—The most important of these is the *mucous patch*. It is most important when it occupies the side of the nipple and the adjacent skin of the areola, for then it is a menace to the sucking infant.

The appearance is typical. It consists of a slightly elevated, glazed, red area, covered, when moist and comparatively undisturbed, with a grayish slime. It can scarcely be mistaken for any other lesion.

A second form of secondary syphilis of the breast is the *diffuse syphilitic mastitis*, a rare condition that sometimes makes its appearance in the latter part of the secondary stage of syphilis. It occurs in either sex, and is characterized by swelling and tension of the breasts, without pain. The organs may be increased in size by a third, and feel nodular. The condition may be mistaken for cancer, but it recovers under anti-syphilitic treatment. If neglected, it does not ulcerate as does cancer, but is followed by a slow and progressive sclerosis.

III. *The Tertiary Lesions.*—The *gumma* is the only one of importance. Thompson in 1920, found that since Lancereaux's work published in 1867, in which six cease were mentioned, only about 40 cases have appeared in the French and German literature. Seventy-five per cent of the cases have occurred in women. One or both breasts may be affected, the lesions being either single or multiple, and varying in size from a pea to an orange. They may be subcutaneous or intra-mammary, occurring in any part of the gland. They form hard, well circumscribed moveable, slowly increasing tumors. There is no pain, and usually no involvement of the axillary lymph-nodes. If untreated, they ulcerate and slough, foul smelling grumous brownish fluid discharging after which appears the typical "punched-out" gumma, with more or less infiltration of its borders. They are not usually adherent to the skin, and are freely moveable, but when deeply seated these characters are disguised, and some breasts have been removed under the suspicion that the lesion was cancer when its circumscription was uncertain, and sarcoma when definite. Need it be pointed out that the personal history of a patient about to be operated upon for cancer ought to be carefully taken, and the possibility of specific infectious diseases considered, and the appropriate examinations made for their elimination?

Gumma of the breast, of course requires no operative treatment; antisyphilitic treatment rapidly effects healing.

It is said that a form of chronic sclerosing mastitis also sometimes occurs in tertiary syphilis. In it, the force of the infection, instead of concentrating at a single focus, distributes over considerable tissue, loses its injurious effect in

a measure, with resulting sub-acute inflammation that terminates in more or less wide-spread sclerosis not unlike the other varieties of syphilitic sclerosis.

ACTINOMYCOSIS

This is a very rare disease of which up to 1914, only 11 primary cases and 16 secondary cases were reported in the literature as having affected the mammary gland. With one doubtful exception, all of the primary cases occurred in women, and of them, one half (5) had nursed children, four of the remaining were married, and only one was single. It is doubtful how the actinomyces fungus enters the breast in the primary cases, but it is supposed to be by way of the milk ducts, and it is on this account that attention is directed toward the number of the patients that had nursed children and therefore had open ducts. However, the statistics are not complete enough to fully confirm this supposition.

Of the 16 cases in which the disease was secondary, the primary seat was in the thorax, the mamma being invaded by extension through the chest wall. One case seemed to be primary in the neighborhood of the mastoid process of the left side, where a furuncle-like lesion developed from which it was found at autopsy that a sinus extended along the external jugular vein. That patient also suffered from metastatic lesions in the liver and kidneys.

So long as the disease is closed, it may be impossible to make the diagnosis, and as in all cases with lumps in the breast, the mistake of supposing it to be cancer may be made. But fortunately suppuration, necrosis and softening occur early with the formation of fistulas and sinuses from which thin watery pus escapes. That is, in itself suspicious, but the final proof of the actinomycotic nature of the disease rests upon the discovery of the "actinomyces grains" in the discharges. These grains, when typical are tiny yellowish bodies, just visible to the naked eye, and occur scattered through the pus. If they are not found, the diagnosis is uncertain, and various treatments tried, and the breast even amputated in the hope of removing the unknown disease; but if they are found, it may be entirely unnecessary to employ any operative treatment as the disease in many cases recovers completely under the administration of iodide of potassium. If, however, as this medication is being tried, new abscesses are found to develop, it may be necessary to open and evacuate them, subsequently draining freely. In the freshly evacuated pus the actinomyces grains should be more numerous than in the discharge from the older sinuses. If the disease does not recover or improve under medication, and if the breast is widely diseased, some surgeons prefer to amputate.

From the reports in the literature it is impossible to determine how many of the primary cases recovered or died. Presumably some of them recovered. Of the secondary cases half died, but they were all the victims of wide-spread infection of the lung and pleura with penetration of the thoracic wall and later invasion of the mamma.

SPOROTRICHOSIS

Of this rare infection we have been able to collect five cases as having affected the mamma either primarily or secondarily. One case was in a man, the others were women. They were all past middle life. In three of them the condition was mistaken for cancer; in one it was associated with cancer. In all the disease was checked by appropriate treatment with iodides given internally, and applied locally, the action of the iodine being so prompt that in two of the cases the lesions disappeared in eight days.

The primary lesion of the disease is usually found to consist of a deep, well-defined, sharply circumscribed, undermined ulceration with a roughened base covered with grayish shining pus, which when wiped away, appears bright red. From such a lesion the disease spreads in all directions as its essential micro-organisms, the sporotricha, are conveyed by the lymphatics.

The general appearance of this lesion is fairly characteristic, but the diagnosis must rest upon the discovery of the fungus, which consists of a delicate mycelium, on the recumbent branches of which, at the points of branching, or at the extremities, spores occur in cylindrical arrangement like cuffs, or in glomeruli, and readily separable from one another. The spores are pear shaped, and attached by very delicate sterigmata. Shed spores are also usually quite numerous, and are ovoid.

If the disease comes under observation before the primary lesion has softened and ulcerated, it may be impossible to recognize it, and the firm lump is mistaken for cancer. So soon as softening occurs, examination of the pus ought to make the diagnosis possible.

THE NIPPLES AND AREOLAE

Congenital absence of the nipples, *bifidity* of the nipples, *imperforate* nipples and *inverted* nipples are all the result of some impediment to, or modification of their developmental stages. They are all very rare, and the surgeon is rarely consulted in regard to them. In case he is, ingenuity is required to successfully modify and make them useful.

The most frequent trouble for which patients seek relief, is *fissured nipples* at the time of lactation. These are not only very painful, but, may be the points of entrance for those micro-organisms by which mammary abscesses is brought about. But in addition to these, some cases are of a nature to grow constantly worse. The latter is especially true when the fissures are situated between the nipple and the areola, where they are most difficult to heal, because the sucking movements of the child's mouth tend to separate their edges and make them larger with each successive nursing. Thus they tend to grow deeper and extend, until they may penetrate the milk ducts, or effect final amputation of the part.

Among 2300 nursing women, Winckle observed 26 cases of *follicular abscesses* of the nipple. In these cases it was frequently necessary to incise the skin to permit the escape of the pus.

Gangrene was observed by Vincent, to follow the application of orthoform to excoriated nipples. On the seventeenth day of this treatment, both nipples were grayish black in color, and one was insensitive. Wallert had a similar misfortune with orthoform, and Du Castel and Nocton saw the same thing result from the application of phenol.

Various *local superficial infections* have been observed to follow contact with the mouths of diseased infants. One of the most frequent of these is "*thrush*," one of the most rare, *diphtheria*. *Pseudo-diphtheria* has been reported. Syphilis has already been mentioned in the section dealing with syphilis of the breast proper.

Sebaceous cysts of the nipple and areola have been observed by some half dozen authors, and Bryant gives case histories of four. He believes that carcinoma of the breast may, at times, have its origin from such lesions. As, however, the cysts are very rare, and the carcinoma very common, and as the former are usually very superficial, and the latter deep, there does not seem to be much of importance in his suggestion.

Pedunculated tumor of the nipple is a rare and interesting formation of which we have been able to collect 33 cases from the literature. In 14 of them the side upon which the tumor occurred was given, and it is interesting to see that 7 were on the right, and 7 on the left side. No doubt several different varieties of tumor have been described under this name, but most of them seem to have been fibromatoids of pedunculated and pendulous form. In one case the tumor was recognized at birth, most of the patients remembered having had the tumor for many years. One patient stated that she had had it from the time of her first menstruation, some 30 years before. When the beginning of the tumors can be recalled, it is usually said that they at first appeared like a wart on or near the nipple, and continued to grow slowly. One case seemed to grow larger with each succeeding pregnancy, two cases with each succeeding menstrual period. All of the patients were women; some were unmarried, most of them married.

In most cases the tumor seemed to embrace the entire structure of the nipple; in six cases it grew from the tip; in two from the side, in two from the base.

Beginning as a kind of wart, the tumor becomes nodular like a berry, or more coarsely nodular like a pine-apple. Some were no larger than a pea, some as large as walnuts, one was as large as the fist. The peduncles were sometimes so short that the growth was almost sessile, sometimes several inches long.

The microscopic examinations that have been made, only serve to confuse us as to the nature of these growths. Thus, they have been described as "fibro-cellular," "fibro-vascular," "fibroma," "hypertrophy of the glands of Montgomery," "erectile tissue," and "angioma cavernosum pendulum mammae."

Vascularity may have caused some to be mistaken for angiomas, and the presence of numerous glands of Montgomery, for glandular hypertrophy.

Except for the traction made upon the pedicles when heavy, and interference with nursing, they rarely cause annoyance.

But upon the convoluted and fissured surface, epithelial cells accumulating in the sulci and depressions, sometimes putrefy, with the production of superficial irritation, and the occurrence of a very disagreeable odor.

FIG. 317.—Pedunculated fibrous tumor of the nipple. (*Jefferys and Maxwell.*)

All of the reported tumors seem to have been perfectly benign. Not one that was removed is known to have returned.

The removal is very simple; under local anaesthesia the peduncle is snipped, any vessels that bleed are ligated, and after the addition of a stitch or two as may be necessary the operation is at an end.

Myoma of the nipple seems to have occurred about half a dozen times. In some cases it reached the size of an orange, and formed a rounded, nodular tumor. Two cases occurred in men.

Microscopic examination shows unstriated muscle tissue, and it is evident that the tumor arises from some of the substance that enters into the base of the nipple at the time of its development.

Sarcome of the nipple was seen by Klebs. He described the tumor he saw as being composed of large spindle cells. It was the size of a half walnut, was situated upon the side of an elongated and thickened nipple and contained large vessels with extraordinarily thin walls.

Intra-cystic papilloma sometimes grows in the ducts of the nipple, where it causes painful swelling usually attended with a bloody discharge, and occasionally by external projection. Very few have been observed. Up to 1917 we were able to assemble but three cases from the literature.

Squamous cell carcinoma of the nipple seems to be more common than the number of reported cases would suggest. It usually assumes the ordinary form of carcinoma spinocellulare, but occasionally behaves peculiarly in that it arises internally from the squamous epithelium that enters the outer part of the ampullae of the ducts, and then grows rather into the breast than externally as a skin tumor. It occurs in both sexes and although a common tumor elsewhere, seems to be rare in this situation.

PAGET'S DISEASE

This, affection perhaps more correctly known by its dermatological designation, *malignant papillary dermatitis*, is thought by some to have been recognized by Velpeau, as early as 1840, but it was Sir James Y. Paget that wrote the first clear description of it in 1874. His contribution begins—

"I believe it has not yet been published that certain chronic affections of the skin of the nipple and areola are very often succeeded by the formation of scirrhus cancer in the mammary gland. I have seen about 15 cases in which this has happened, and the events were in all of them so similar that one description may suffice."

In the somewhat lengthy description that follows, the salient features are given as (1) occurrence in women from 40 to 60 years of age; (2), first appearance upon the nipple or areola in the form of a florid, red, raw surface, very finely granular, as though the whole thickness of the epidermis was removed, and resembling a very acute diffuse eczema. From the whole of this surface there is a copious clear viscid exudation. There are tingling, itching and burning sensations. (3), The disturbance was never seen to pass beyond the areola, and only once effected a deep excavation like rodent ulcer. In some cases the disease progressed like chronic eczema, in others was more like psoriasis. (4), Cancer of the mamma followed in a year or two there being nothing peculiar about the tumor which developed beneath and not far from the affected skin, from which it always seemed to be separated by an interval of healthy tissue. The cancers were sometimes acute, sometimes chronic, followed the usual course, tended to the usual end, affecting the lymph-glands and distant parts,

and showing nothing that might not be written in the ordinary history of cancer of the breast.

To Paget, to many later, and to some present day surgeons and pathologists, the disease is a clinical entity with fairly definite manifestations; to pathologists, and to most dermatologists, it is a definite pathological entity with characteristic histological changes.

Some 300 cases are recorded in the literature, of which about 250 sufficiently conform to the original description to be regarded as the real thing.

Many pathologists and most dermatologists follow Paget in believing that the disease begins in the skin, and is a skin affection primarily; many surgeons, a few pathologists, and very few dermatologists follow Handley who believes that carcinoma of the breast is the parimary affection and that the skin is secondarily invaded.

If there was any certainty that the cases reported as Paget's disease were clinically and pathologically identical, or in comparable stages, there might be less difficulty in determining the true nature of the disease, but there is not. Among the cases clinically diagnosticated Paget's disease, and brought to us as such, there was one case of carcinomatous ulceration of the skin, one case of squamous cell carcinoma of the nipple, and one case of ulceration of unknown nature, but not Paget's disease.

The publication, by reliable dermatologists, of some twenty cases of Paget's disease occurring elsewhere than upon the breast, might be supposed to be sufficient to prove that the disease originates in the skin. When localized upon the back, arm, buttock, glans penis, etc., beneath which no cancer could occur, the disease cannot result from the upward extension of cancer into the lower layers of the skin. But this seems to be persistently overlooked by those unacquainted with the finer details of the disease. Of 18 cases of extra-mammary Paget's disease collected by Hartzell, 9 were situated upon the genitalia, five being upon the glans penis. They differed but little, if at all from the disease as it occurs upon the breast.

The time that intervenes between the appearance of the Paget's disease and the occurrence of the carcinoma ought also to be taken into account. Paget stated this to be from one to two years, but later observers have found it rare that cancer supervenes so early, and Darier observed a case in which the appearance of the tumor was delayed for ten years, and Jamison one in which it was twenty years.

If the cancer originated from the cells of the diseased skin, it ought to follow one of the recognized types of squamous cell carcinoma, but it does not; as Paget himself recognized, it is the ordinary form of mammary cancer, carcinoma rotundocellulare and carcinoma cylindrocellulare having been observed, but never carcinoma squamocellulare. The relation of the skin disease and the cancer is not like that of lupus vulgaris and cancer. In the latter, the cancer is definitely the result of the chronic irritation, or of associated infection, and the cancer grows from the disturbed tissue, with the expected result. In the former, the cancer develops from a neighboring structure, through means not easy to understand. It develops from the gland, and if there be no subjacent gland,

there never is any cancer. Paget's disease upon the penis or scrotum is very destructive, but is never followed by carcinoma.

Were it not for the certainty with which typical cases of Paget's disease are followed by carcinoma, it might be suspected that the relation was only accidental and the result of the general frequent occurrence of carcinoma; but the association is too definite to permit such a thought. If it could be shown that the cancer was always already present when Paget's disease appears, it might be
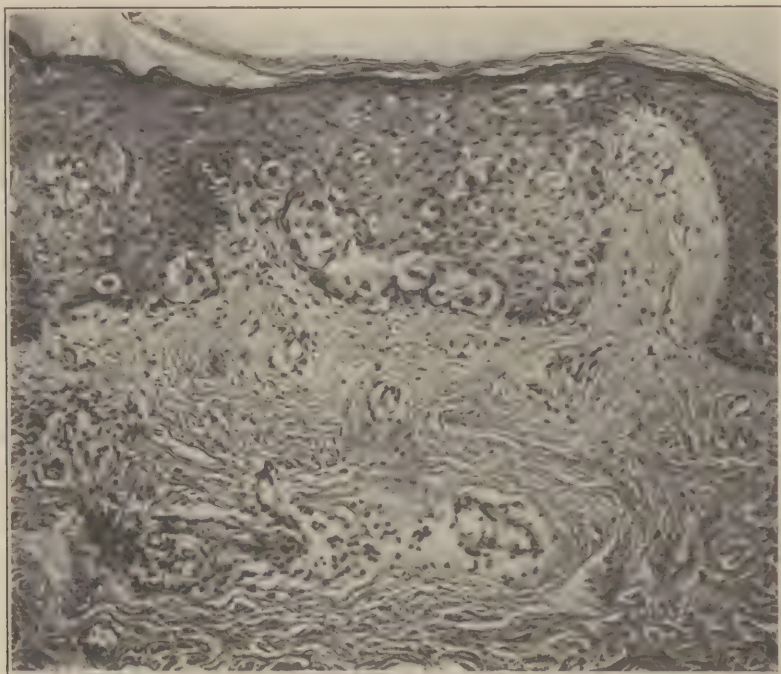
FIG. 318.—Microscopic section of Paget's disease of the breast. The typical vacuolation of the lower layers of the epidermal cells is well shown in the upper middle portion of the section. (*Photomicrograph by Dr. F. D. Weidman.*)

supposed that the latter resulted from the escape from the nipple of something irritating by which the skin was affected; but that is impossible because of the care with which breasts affected with Paget's disease are examined for cancer, and the regularity with which it is absent in fresh cases, as well as by the many years that may elapse before the skin affection is followed by the cancer.

Butlin, who studied some of Paget's cases, thought that he observed changes in the ducts that were comparable with those in the epidermis. Bowlby examined 13 cases the lesions in which he describes as follows.

"The process originates in an inflammation of the derma, with small-cell exudate beneath the epithelium. The latter in its turn, is implicated, its cell being loosened from one another by fluid exudation, and finally cast off. The derma being exposed, the inflammatory process advances more rapidly, and proceeds to the formation of pus, and the destruction of the true skin. The inflammation now extends along the ducts, causing their epithelial linings to pro-

liferate, the cells sometimes collecting in masses which fill the tubes. Following this there is a tendency for the epithelial cells in the acini or ducts, to grow out into the surrounding tissue and to take on cancerous growth, an event which is generally preceded by inflammatory changes in the connective tissue stroma of the mamma, indicated by exudation of leukocytes and fibrous thickening. The cancerous growth is sometimes directly continuous with the nipple, but is more often separate from it and deep in the breast. It is usually a spheroidal celled carcinoma, though columnar celled tumors have been described."

A microscopical examination shows, in the epidermis, numerous round or oval vacuolated cells, which are most numerous in the superficial layers of the epithelium. These cells are of constant occurrence in the disease, but are not absolutely peculiar to it, being occasionally present in other inflammatory conditions of the epidermis. Paget's disease must not be confused with an eczematous condition of the nipple which is sometimes seen as a sequel of cancerous growths and which appears to result from some irritating discharge from the ducts."

From our own studies we have been led to suppose that the earliest changes in Paget's disease consist of a lymphocytic and plasmacytic infiltration of the corium, soon followed by looseness and apparent weakness of the resisting power of the tissue, that permits the epithelial pegs of the rete to extend downward a short distance, and their cells to separate slightly. The separated cells do not tend to become invasive, but loose the prickles by which they usually hang together, swell and transform into large, pale and vacuolated bodies that Darier and his followers supposed to be "psorosperms." The described changes seem to begin in the prickle cell layer, and extend both upward toward the surface, and downward to the Malpighian layer. The affected cells become almost double the normal size, clear, hyaline, smooth on the surface, and contain the relic of a nucleus that varies from a swollen vesicle to a shrunken remnant pushed to one side, and not infrequently showing a "seal-ring" appearance. In the early stages such cells seem to be scattered among many normal cells, but as the disease advances, they form the greater number of cells present. The vacuolization and hyalinization seem to destroy the keratin forming power of the cells, so that no horny layer of epidermis is formed, and as the power of multiplication seems to disappear with that of differentiation, the cells are not replaced as rapidly as they desquamate, and the cuticle becomes thinner and thinner, the papillae flattening out, the epithelial pegs shortening and then disappearing, until the surface becomes covered with a very thin layer of epithelium, much changed in appearance, and sometimes absent altogether. As the epithelial layer thins more and more, it becomes less and less efficient as a covering and protection, so that oozing of lymph takes place, and drying upon the surface, covers it with a yellowish brown crust.

The swollen and vacuolated Paget's cells have been the source of much speculation. As has been said, Darier supposed them to be protozoan parasites, Jacobeus imagined them to be carcinoma cells that had wandered from the milk ducts between the epidermal cells. But they do not bear the slightest resemblance to cancer cells, and Winiwarter has been able to discover all of the intermediate stages between the normal and vacuolated epidermal cells.

THE MALE URO-GENITAL ORGANS

The disturbances of greatest surgical interest in this system of organs center about the neck of the bladder, and the adjacent part of its posterior and inferior wall known as the *trigone*. This triangular area, bounded anteriorly by the orifice of the urethra, and posteriorly and laterally by the orifices of the ureters, is not formed from the tissues of the uro-genital sinus, but from the lower portion of the Wolffian ducts spread out and flattened. It is of mesenchymal derivation, as contrasted with the remainder of the vesical wall, which is endodermal. To the naked eye the area, included in the triangle is paler in color than the rest of the bladder wall, and though sometimes streaked never has any rugae. Its epithelium, a transitional squamous tissue, is mesodermal, that of the rest of the bladder endodermal. The tissue of the trigone is continued anteriorly to form the floor of the urethra so far as the orifices of the ejaculatory ducts, in its prostatic portion. A longitudinal fold of mucous membrane arises from the lower anterior part of the trigone, and descends a short distance into the urethra. It is the *uvula vesicae*. Just beyond it, and sometimes continuous with it, in the prostatic portion of the urethra, is another longitudinal ridge about 2 cm. in length of a somewhat clavate form, the thick end of the club being at the upper or posterior end. It is variously known as the *verumontanum*, the *caput gallinaginis*, or the *colliculus seminalis*. On each side of it a more or less marked depression is known as the *prostatic sinus*, the floor of which is made slightly porous through the numerous openings of the prostatic glands. In the middle line, just in front of the verumontanum is a larger and deeper depression, the *sinus pocularis*, or, as it was called by its discoverer, Weber, the *uterus masculinus*. It is the anatomical homologue of the female uterus, and like it is derived from the lower extremities of the conjoined Müllerian ducts or tubes. Into it the ejaculatory ducts open as little slit-like orifices.

About this portion of the urethra the *prostate gland* forms, beginning during the third month of embryonal life, according to Pallin, through three sets of buds arising from each side of the urethra. Lowsley, thinks the organ has its origin in five principal sets of buds or evaginations.

McMurrich describes these as consisting of "a middle group arising from the floor of the urethra above the entrance of the ejaculatory ducts, a posterior group also from the floor, but below the openings of the ejaculatory ducts, two lateral groups from the sides of the urethra and floor of the grooves on either side of the colliculus seminalis, and an anterior group, smaller than the others, from the urethral roof. Each of these groups gives rise to a lobe of the prostate, the posterior becoming more definitely circumscribed than the others because of the formation about it of a definite capsule. A few scattered outgrowths arise from the floor of the urethra above the middle group, but as a rule, these attain only a slight development. The muscular tissue so characteristic of the gland

in the adult male, is developed from the surrounding mesenchyme at about the fourth month."

All of these rudiments of the prostate do not develop uniformly, nor do they all mature. The tubules of the anterior lobe reach their maximum by about the 20th week of embryonal life, and then proceed to retrogress, so that by the 30th week they are reduced to about one-half of their former size, and are almost absent at the time of birth.

Lowsley believes that the middle lobe develops independently of the others, but most authorities think that the middle lobe develops from the lateral ones.

The primitive buds probably vary from 15 to 50, if their number can be estimated by counting the excretory ducts that open into the prostatic sinus. At first they are all solid, but later they become hollowed out and each is provided with a lining of cylindrical epithelial cells, that usually appear to be in single layer, though Langerhans states that a double layer is present in all of the prostatic alveoli.

The ducts branch again and again, forming the parenchyma of the prostate gland, and about them the fibro-muscular stroma collects so as to form an organ customarily described as consisting of an anterior, a posterior, a middle, and two lateral lobes. Wilson and McGrath, however, through a more exact method of study based upon the grouping of the glandular structure rather than upon mere external morphology, find the organ composed of two symmetrical peripheral lobes—the lateral lobes—an interposed middle lobe, and a small anterior one.

It is through this organ that the first part of the urethra, and especially that part of it derived from the Wolffian ducts, passes, beginning in a short infundibulum pointed downwards and forwards towards the triangular ligament where the prostatic portion ends and the membranous portion begins.

From the complex development it may be correctly surmised that the neck of the bladder and the surrounding structures are occasional seats of congenital defects, and that any tumors arising from them, may occasion obstruction.

The prostatic urethra is also subject to occasional invasion by micro-organisms ascending from the more anterior urethra, that may then find their way into the glandules of the prostate, into the seminal vesicles and vasa deferentia, or entering the bladder itself, eventually ascend the ureters to the kidneys that may then become diseased.

The most potent factor is gonorrhoea.

The infectious agents, entering the external urinary meatus, seem, as a rule to effect little disturbance in the fossa navicularis, unless the squamous epithelium with which that portion of the canal is lined be abnormal. Instead, they pass more deeply and entering the part of the canal lined by columnar cells, excite a catarrhal inflammation with purulent exudate. It seems as though the activities of the gonococci themselves were largely limited to the surface, but their inroads are almost invariably accompanied by staphylocci, which penetrate into the glands of Littré, which not infrequently suppurate, so that a considerable degree of periurethritis results. It is probably in the recovery from these lesions that cicatrization results in the obstructions known as *strictures of the urethra*. If the urethritis remain confined to the anterior part

of the urethra, the strictures will be in the penile or pendulous portion, but if the infection extend posteriorly, as is frequently the case, they occur in the membranous portion, where they are, in fact, most common. The strictures consist of annular formations of connective tissue, by whose contraction the canal is greatly reduced in calibre, of transverse bands, and of kinks, any or all of which may obstruct the passage of the urine. The almost inevitable result being that the bladder is called upon to exert more powerful muscular efforts in order that the urine be voided. Two secondary results follow: the bladder hypertrophies; and the portion of the urethra behind the seat of obstruction becomes dilated.

To the consequences of the hypertrophy of the bladder, return will be made later.

If the inflammation extending backwards reach the prostatic urethra, the infectious agents commonly reach the prostatic ducts, into which the disturbance may extend, so that acute prostatitis, followed in some cases by abscess of the prostate not infrequently results. Going still farther back, cystitis results from the presence of the infectious agents, and though the inflammation thus produced is usually acute, it seems to be occasionally followed by disturbances of enduring character.

It is not certain that the conditions next to be described are the result of antecedent gonorrhoea, but many believe them to be closely interrelated.

1. Median Bar Formation

Median bars are obstructions at the vesical outlet occasioned by a transverse fold or "bar," partly composed of mucous membrane, partly of cicatricial tissue, and partly of glandular tissue derived from the sub-cervical glands of Albarran. The first to call attention to them seems to have been G. J. Guthrie, who in 1834, in his Anatomy and Diseases of the Neck of the Bladder, speaks of them as "Bars or Strictures of the Neck of the Bladder."

Except for one writer, Mercier, who wrote some half dozen papers, in which he spoke of "Valvules du col de vessie," little attention seems to have been paid to the matter for some 60 years, at the end of which time the cystoscope was invented, and the French school of urologists under Guyon brought the subject once more to the fore, describing the condition as "Prostatisme sans prostate." In this country, the writer through whose work the condition has become best known is Alexander Randall.

The symptoms resulting from the presence of the lesion so closely resemble those of urinary obstruction from prostatic enlargement, that it is a surprise to find upon examination that the patient has no enlargement of that organ, but in many cases exactly the reverse, atrophy. To discover the frequency of occurrence, the mode of origin, and the variety of appearances presented, Randall examined the bladders of 300 male cadavers that came to autopsy in the Philadelphia General Hospital, for all causes, whether with symptoms suggesting urinary disturbance or not. Median obstructions to the vesical outlet were found in 18% or 54 cases, and upon microscopic examination were found to be fibrous in 10% and glandular in 8%.

But, Randall, although he admirably gives us the gross morbid anatomy and pathological histology of the condition, is not so clear about its meaning. Guthrie, who first described the bars, spoke of them as "unnatural elevations of certain fibrous structures which underly the mucous membrane at the posterior or vesical limit of the urethra, but which is unaccompanied by and unconnected with any enlargement of the prostate." Civiale, described the bars as "simple membranous folds, smooth, thin and almost transparent," or as "like the free edge of a fold in the form of a rounded cord." In the latter case the barrier is thicker and between the two layers of the mucous membrane there

Fig. 319.—Median vesical bar of the fibrous type, short and thick with distinct shortening of the urethral region, the verumontanum being drawn up directly under the base of the bar. The patient was a man of 60 who died of pneumonia and nephritis in the Philadelphia General Hospital. (*Randall.*)

is a dense and resistent tissue analogous to that of the vesical sphincter except that the one under consideration is sclerotic and the other muscular."

Mercier in his later writings described two types of bars: "muscular" and "prostatic."

Sir Henry Thompson recognized the bars as derived from some kind of outgrowth from the prostate. The French school of urologists came to the conclusion that they had nothing to do with the prostate, but were due to changes in the muscular wall of the bladder, and in this opinion were supported by von Bergmann and Albarran, as well as by Ciechanowski.

Chetwood decided that the whole trouble was due to fibrous thickening of the tissues about the neck of the bladder.

As the prostate was frequently found, at operation, to be smaller than normal, the German school came to the conclusion that the whole matter was

referable to atrophy. Randall seems to have shown that the majority of the cases are to be referred to changes initiated in the prostate.

The presence of the band, and the resulting obstruction lead to the formation of a *bas fond*, or pouch, in which some of the urine is retained, the bladder never being entirely emptied at micturition. There is, therefore, always some residual urine, and the patient's trouble increases in proportion to its quantity. The bladder tends either to hypertrophy on account of the increased effort to rid itself of the accumulation, or, it distends, being unable to satisfactorily compensate. Its wall becomes reticulated, and thickened, and not infrequently diverticulated. The ureters become affected and later dilated, the obstruction and dilatation extending to the kidneys, so that hydronephrosis may occur. As the urine is constantly in danger of infection from catheters and sounds introduced for the purpose of drawing the water, or for exploration, infection soon becomes inevitable, the urine carries the micro-organisms into the ureters, and the hydronephrosis becomes pyonephrosis, and the patient dies of uremia.
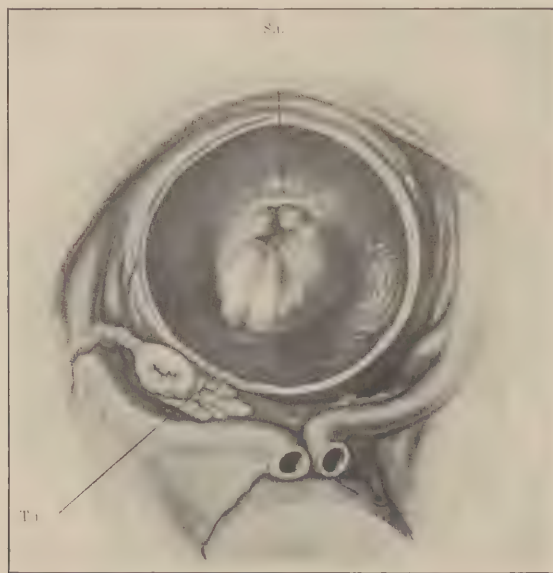
FIG. 320.—Hypertrophied prostate projecting into the bladder. Viewed from above. *S.i.*, Prominence of the sphincter urethra internus; *T.i.*, torus interuretericus. On both sides of the urethral openings are small hypertrophies arising from the submucous gland. (*Tandler and Zuckerkandl. Published by Dr. Werner Klinkhardt, Leipzig.*)

2. ENLARGEMENT OF THE PROSTATE

According to the descriptions given in most of the text-books, the prostate gland is chestnut shaped. Wilson and McGrath describe it as an "oblate conoid," the base directed upward and backward, the apex downward and forward, resting upon the triangular ligament. Its size from base to apex measures from 33 to 45 mm., averaging 34 mm. Its transverse diameter varies from 34 to 51 mm., averaging 44 mm., the thickness varies from 13 to 24 mm.,

averaging 15 mm. and its weight varies between 13.7 and 21.3 grammes, averaging 16.5 grammes.

The general structure, based upon embryological grounds, consists of four lobes: two symmetrical, peripheral or lateral lobes, an interposed middle lobe, and a small anterior lobe.

The organ is pierced by the urethra, which traverses it vertically, forming a slight curve, the course of which is slightly sigmoid, with the concavity directed forward in the upper third, and backward in the middle third, and by the two ejaculatory ducts on their way from the seminal vesicles to the prostatic sinuses

FIG. 321.—Sagittal section through the pelvis, showing an enlarged prostate. *B.u.*, Bulbus urethralis; *C.g.*, caput gallinaginis; *L.a.*, lobus anterior; *L.m.*, lobus medius; *R.r.*, recessus retro-utericus; *V.s.*, vesicula seminalis. A short probe projects from the ejaculatory duct. (*Tandler and Zuckerkandl. Published by Dr. Werner Klinkhardt, Leipzig.*)

in the floor of the prostatic portion of the urethra, passing obliquely forward on each side between the middle and lateral lobes.

The organ is surrounded by a firm closely adhering fibrous capsule, and is held in the position by a dense fibrous tissue which Retzius has called the *ligamentum pelvio-prostaticum capsulare* partly composed of enveloping fibres, and partly of diverging bands, the *ligamenta puboprostatica*. The posterior surface is intimately blended with Denouvillier's fascia, and on this account the organ cannot be completely enucleated with ease.

Although the prostate is a muscular organ and surrounds the urethra, it does not participate in the formation of the sphincter muscles by which that tube is closed. The internal sphincter which encircles the commencement of the tube is derived from the deeper layer of the muscular sheet of the trigone: the external sphincter, which surrounds the urethra at the apex of the prostate, is

composed of striated muscle fibres partly derived from the compressor urethra muscle.

The unstriated muscle of which the greater part of the organ is composed, seems to exist solely for the purpose of expressing the secretion from its glands. Of the latter there seems to be a variable number, as different anatomists have counted from 15 to 50, each provided with its own duct. As the ducts descend from the floor of the urethra where they open, into the depths of the gland, they branch again and again, until they terminate in spaces variously regarded as tubules and as acini by different histologists. These seem to be lined by a single layer of columnar epithelial cells, though there are certain good authorities who believe that there are always two superimposed layers. We have not been able to substantiate this view.
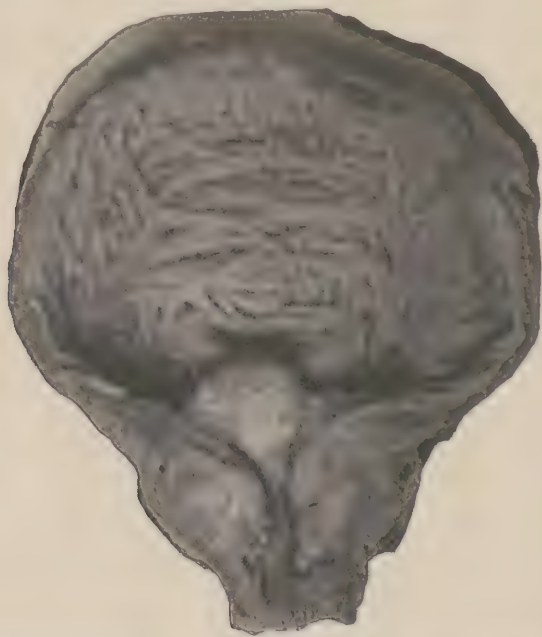
FIG. 322.—Prostate hypertrophy. The bladder and the urethra are laid open permitting the middle enlarged lobe of the prostate to be seen projecting upward like a rounded fungus. (*Aschoff.*)

From the ducts numerous tiny diverticula are given off from time to time, so as to increase the quantity of glandular tissue. In all, about one half of the substance of the normal prostate seems to consist of glandular tissue. But the proportion differs in different individuals, and it is uncertain whether age or physiological condition may not modify the structure, as in the mammary gland, which the prostate in some measure resembles. The epithelial cells were found by Wilson and McGrath to rest directly upon the unstriated muscle tissue, no membrana propria being demonstrable.

Here and there in the substance of the organ islands of lymphoid tissue may be found. They are not constant, vary in different cases, and may be absent.

It should be no surprise to learn that in certain cases of posterior urethritis the gonococcus, followed by secondary invading micro-organisms easily find their way into the crypts of the glandular structure of the prostate and effect inflammatory disturbances that not infrequently become chronic. It is as a sequel of these conditions that many regard the condition known as "enlargement of the prostate," or as others call it, "hypertrophy of the prostate." It is so common that about one third of all male cadavers examined at autopsy are found to have it in some degree. Now biologists regard conditions that occur as frequently as 30% as normal, so that with reference to enlargements of this kind, it at once becomes a question whether they may not be normal and merely a manifestation of age, except in cases exceeding a certain limit. The various theories of origin collected by Wilson and McGrath are as follows:

1. Prostatic enlargement may be a family inheritance.
2. It may be a normal phenomenon of senility, which is supposed on account of its rarity before the 50th year of life.
3. It is a condition analogous to fibroid tumors of the uterus.
4. It is a disease of excessive alimentation—alcoholism, constipation, etc.
5. It is a result of the hyperemias incidental to sexual excesses.
6. It is a consequence of gonorrhoea, prostatitis, etc.
7. It is an end result of general febrile disease—tuberculosis, rheumatism, gout, etc.
8. It is due to arterio-sclerosis.
9. It is a compensatory process designed to effect hypertrophy of the bladder.
10. It is neoplastic.
11. It is due to the absence, in declining sexual life, of some internal secretion from the testis which normally regulates—inhibits—the growth of the organ.
12. It is a compensatory provision to supply a stimulus to a testicle with declining function.
13. It is a hypertrophy caused by urethral stricture.

To these must be added at least one other.

14. It is a phenomenon of involution similar to what goes on in the mammary gland after lactation.

Not one of these various theories has proved satisfactory upon continued investigation, however, although the infectious and inflammatory theory seems to have most in its favor.

Wilson and McGrath examined 468 enlarged prostates, 378, or 83% being hypertrophies. All of the patients from whom they came were above 50 years of age, and 83% were over 60. Seventy-eight per cent were married men; 18% were widowers; 4% were single. In only 70 of the 378 cases was the parenchyma increased without apparent increase of the stroma; but in 17 the stroma was increased without any recognizable increase of the parenchyma. In 300 there was increase of both. In 205 there was notable increase of the muscle. In 266 cases, either diffuse or circumscribed round cell infiltrations were present.

According to these writers hypertrophy of the prostate, so-called, represents an enlargement and change of form, caused by an increase in the volume of its individual tissue elements, that is, of the normal morphological factors of the organ, and not by the production of heterogeneous elements.

"When a freshly hypertrophied prostate is sectioned grossly, the parenchyma, if increased to any considerable extent, bulges above the cut portion of the stroma, presenting, usually, a number of whitish nodules between which are yellowish, or yellowish red succulent areas which

on slight pressure exude a cloudy yellowish juice. This may, in turn, contain a greater or less amount of yellowish brown or black granules, the corpora amylacea."

"Tandler and Zuckerkandl, as the result of dissection of 42 cases, came to the conclusion hypertrophy of all parts of the prostate does not exist. In the most pronounced hypertrophy they always found certain parts of the organ atrophic. In their series, hypertrophy of the posterior lobe was not once observed, and in none was the middle lobe entirely free from hypertrophic change.

"They conclude that hypertrophy affects without exception, the portion of the prostate that is turned toward the bladder, and on that ground they recommend operation by the vesical route."

The sequence of events in enlargement of the prostate, according to Wilson and McGrath, is as follows: "There is an initial hyperplasia of the parenchyma, marked microscopically by

FIG. 323.   FIG. 324.

FIG. 323.—Prostatic hypertrophy. Longitudinal section through the bladder, prostate and urethra. The enlarged middle lobe projects behind the urethra, into the bladder, in form not unlike a rounded fungus. (*Aschoff*.)

FIG. 324.—Prostatic hypertrophy. The bladder, prostate and urethra are cut longitudinally. The urethra makes a right-angle kink in passing through the enlarged prostate. (*Aschoff*.)

high cylindrical epithelium with swollen nuclei, which resembles, in all other respects, the actively secreting epithelium in other well studied glands. That those epithelial cells are actively secreting, is further shown by the presence in early stages, of relatively large amounts of secretion, which is distinguishable grossly from that of the normal prostate. This parenchymatous hypertrophy is frequently so great as to result in the development of infoldings of and papilliferous proliferation from the alveolar walls, sometimes carried to the extent of completely bridging the alveoli."

"Apparently the second stage of hyperplastic development, though not a definitely limited one, is that of retention within the alveoli and tubules, of the secretion. This retention may be due to beginning exfoliation of the epithelium, and it may be due in part to blocking of the excretory ducts by a beginning concomitant muscular hyperemia."

"The third stage is parenchymatous degeneration, which in the hypertrophied prostate is marked by atrophy and exfoliation of the epithelium. The first of these processes is shown by the flattening of the epithelial cells, the reduction in the size of the nuclei, and the diffuse staining of the cytoplasm. The second process, exfoliation may, and frequently does occur in the epithelium which is still in the high columnar secreting phase. Atrophic epithelium is usually associated with swollen cystic acini. Exfoliation may be so extensive as to present a picture of completely denuded alveoli or cyst walls. Exfoliations may occur in any acini, but are densest and best preserved in large acini. The stripping of the epithelium from the papilliferous projections and alveolar bridges leaves these as slender fibrous projecting or bridging structures."
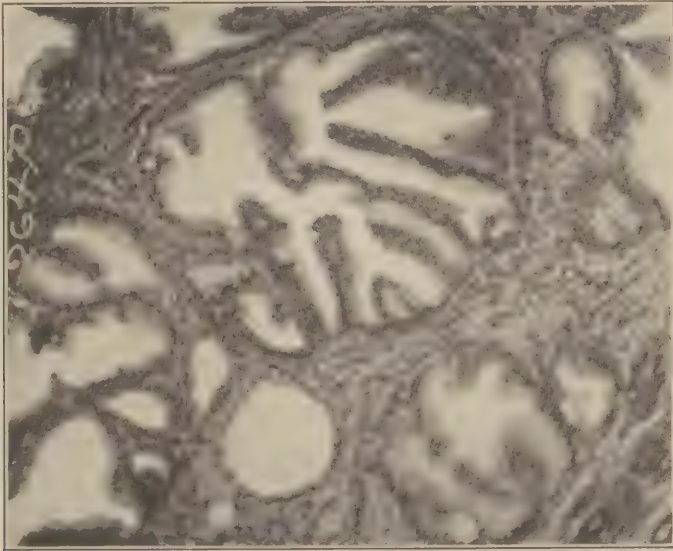
Fig. 325.—Parenchymatous hyperplasia of the prostate. (*Wilson and McGrath.*)

"Early in the development of the parenchymatous hyperplasia, there begins a muscular outgrowth which represents, apparently, an attempt on the part of nature to expel from the gland the retained secretion. Our cases, however, do not show a large percentage in which the muscular hyperplasia greatly outweighs the element of fibrous connective tissue overgrowth."

The overgrowth of fibrous connective tissue in the hypertrophied prostates in our series, is the most constant factor, though it must be born in mind that many cases coming to operation may fairly be assumed to have long passed the stage of active parenchymatous and muscular hyperplasia."

From these quotations it will be clear that Wilson and McGrath regard the parenchymatous change as primary, and the musculo-connective tissue changes as secondary. Keen and Brooks, after a careful study of 58 cases became convinced that the hypertrophy is really of inflammatory origin.

It does not necessarily begin uniformly in all parts—in fact it probably rarely does so—but may show itself in any part, least frequently in the anterior or ventral lobe. To the naked eye it may first show itself as enlargement of some group of glands, and if it for a time remains localized in them, causing increase in their size, with outward displacement of the surrounding fibro-muscular tissue the result may suggest a growing benign tumor—indeed, such localized glandular hyperplasias have frequently been described as adenomas, and not a few writers

attribute the whole of the enlargement to the development of the "adenomas." It goes without saying that they are hypertrophies of antecedent glands, and are in no manner related to tumors.

Nor does the hypertrophy always end by uniformly affecting the whole gland. It may affect one or both lateral lobes, or one or both of them together with the median lobe. Not infrequent are cases in which the hypertrophy is limited to the middle lobe.

Those cases in which only the lateral lobes are affected are unlikely to give severe clinical manifestations until late, because they trespass least upon the vesical orifice. Those cases in which it begins in the middle lobe, or in which the
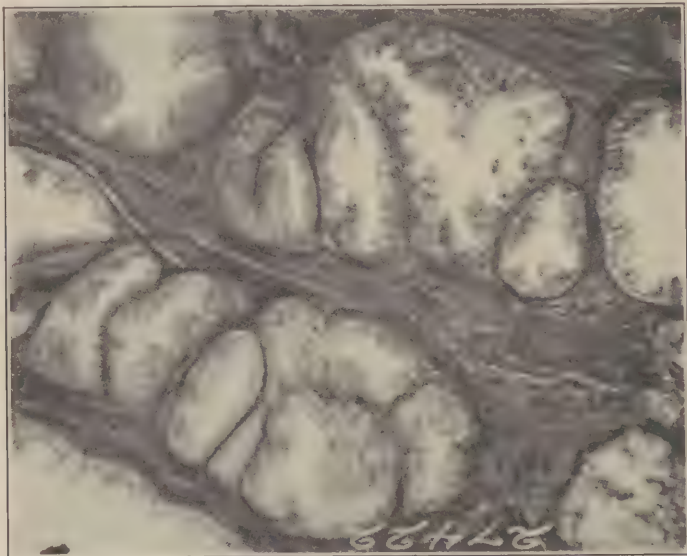
FIG. 326.—Parenchymatous hypertrophy of the prostate. (*Wilson and McGrath.*)

middle lobe enlarges early, show disturbances of the urethral orifice very early, and may leave some doubt as to whether the obstruction depends upon prostatic disease, or upon median bar formation without prostatic disease.

The greatest resistance to the growth of the gland is found in the anterior and downward directions, hence the enlargements are usually directed backward and upward, with the result that the prostatic portion of the urethra becomes compressed, elongated and flattened, or pushed toward one or the other side, or all of these. If the size be considerable, and the vesical outlet elevated to a marked degree, a post-prostatic pouch will be formed, and that part of the bladder composing it will be at a lower level than the urethral orifice—"*bas fond.*" From this, urine will be expressed with difficulty, and soon residual urine collects in it in quantity increasing as the prostate continues to enlarge and the obstruction at the urethral orifice more difficult to overcome. Events now follow one another as described in the section dealing with the median bars. The position of the urethral orifice, and the obstruction at its beginnng, make it difficult for the patient to begin to pass the water; the dislocation and distor-

tion of the canal, as well as the obstruction, cause the flow to be slow and sometimes painful. The sphincter muscles of the bladder being disturbed and more or less dislocated, stoppage is slow and imperfect, and final drops trickle, while the residual urine in the *bas fond* gives the correct sensation of not having emptied the bladder. With this residual urine added to the quantity secreted and conveyed to the bladder, the patient may be obliged to get up at night to relieve himself, with increasing frequency as time goes on and the condition gets worse. Later come attacks of retention which make catheterization necessary. In the meantime the bladder attempts to compensate for the obstruction by
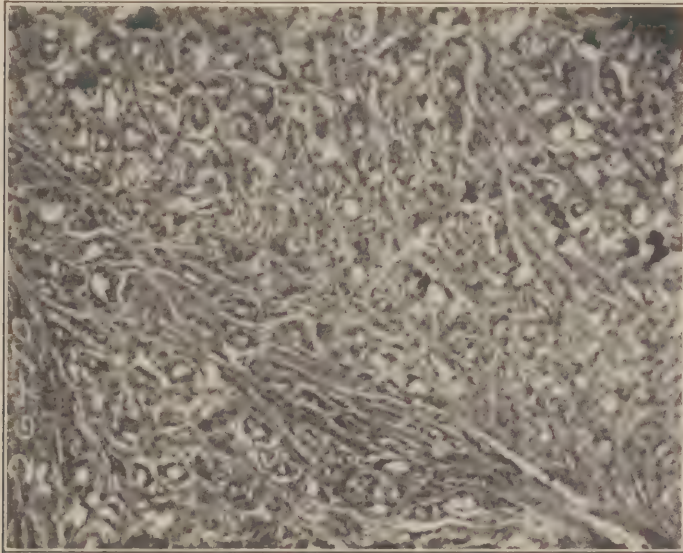
FIG. 327.—Adeno-carcinoma of the prostate. (*Wilson and McGrath.*)

hypertrophy of its muscular wall, and so long as this is successful, the patient does not suffer serious discomfort, but as this power is limited, the bladder, having greatly increased in thickness and no longer able to maintain a strength proportional to the increasing obstruction, begins to yield, and its wall that has been fairly smooth, now begins to show a distinctly trabeculated and reticulated muscular structure as it dilates, and the muscular bundles become separated more and more widely from one another. Upon holding such a bladder against a light, one is sometimes surprised to see how thin is the wall between these muscular bundles, seeming to consist of nothing but the mucous membrane. It not infrequently happens that local areas yield to the intravesical pressure, and bulge. How frequently this occurs during life cannot be told except in cases in which the bulging takes place so regularly at a single point, and with such secondary changes as to cause a permanent diverticulum to form.

These are quite common, and may be single or multiple, and are usually situated upon the posterior wall, though they may be anywhere. They may also be either small or so large as to exceed the bladder itself in size. It is such

diverticula that have been described as double bladder, cyst of the bladder, divided bladder, etc. From the diverticula the urine escapes even less readily than from the obstructed bladder, and they are common seats for the formation of calculi. In other cases the bulgings take place much more widely, and in great numbers, though of small size. Tiny diverticula thus are formed, and are sometimes known as "cells." They are too small to collect and retain urine, but become the collecting points of any kind of solid particles the diseased urine
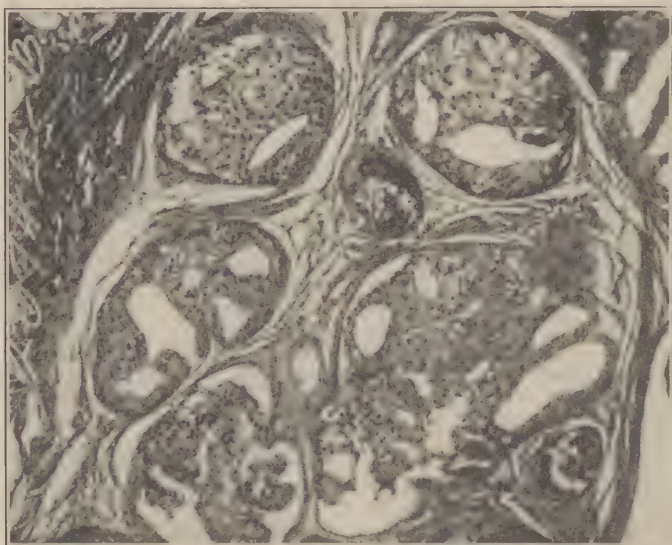
FIG. 328.—Duct carcinoma of the prostate. (*Wilson and McGrath.*)

may come to contain, about which its salts later become deposited, so that small calculi are formed.

With the increase in the thickness and muscular strength of the vesical wall, come disturbances of the ureteral orifices. It will be remembered that the lower ends of the ureters pass diagonally through the bladder wall, in such manner as to serve a valvular function. When the bladder wall contracts, the internal pressure compresses the intra-mural portion of the ureters, and prevents the regurgitation of the urine toward the kidneys. As the bladder undergoes hypertrophy and its walls thicken, the effect of this mechanism is usually conceived to be intensified, and the result is not only the prevention of regurgitation, but a continuous partial obstruction of the ureteral meatuses that makes it difficult for the urine to escape from the ureters into the bladder, retains an increasing quantity of it in the ureters, dilating them, and then the renal pelves, and finally occasioning compression of the kidney substance until its pyramids are flattened out, and it slowly becomes resolved into a kind of sac apparently composed chiefly of the cortical substance, and no longer able to perform its function. This condition goes by the name of *hydronephrosis*.

It is, however, possible that hydronephrosis may be caused through another mechanism. In cases of urethral obstruction, and especially those situated

at the vesical outlet, with hypertrophy of the bladder, it seems that sometimes the hypertrophic changes miscarry as regards the described valvular action of the contracting bladder wall, and the ureters remain open so that the urine can and does regurgitate. It would seem as though this mechanism really better explained the condition than the other as the forcible regurgitation of the urine under the pressure of the hypertrophied bladder, ought to be far more effective in occasioning the destructive dilatation than the mere interruption of the outflow of the urine from the ureters during the act of micturition.

Fig. 329.—Carcinoma of the prostate (⅔ natural size). *a*, Tumor nodules in the neck of the bladder; *b*, hyperemic mucosa of the bladder wall; *c*, lateral lobe of the prostate (not carcinomatous); *d*, colliculus seminalis; *e*, urethra. (*Johres*.)

We are sure that we have frequently seen, at autopsies performed upon prostatic patients and others with similar obstructions, ureteral orifices that gaped permanently, and were in no way obstructed as regarded urinary outflow, but were, unfortunately for the patient, not closed during micturition, so that regurgitation must always have taken place.

The almost inevitable infection of the urine of the obstructed bladder soon reaches the ureters and ascends to the kidneys causing pyelonephritis which results in death.

The mode of ureteral infection, and its ascent to the kidney is a mysterious matter. If the ureteral orifices were so changed by disease as to permit the regurgitation of the urine as described above, nothing would seem to be more easy to account for than the infection of their contents, and the later infection of the kidneys. But if the earlier mechanism be the one operative in the case, and the ureters are obstructed, the admission of the infectious agents ought to be difficult, and ascent to the kidneys late if it occurred at all. But as a matter of fact, the extension of the infection from the bladder to the kidneys does not seem to take place in this direct manner. At least, it is difficult to prove experimentally that it does. Instead, the path of infection seems to follow the course of the lymphatics from the bladder to the kidney. Interesting experiments proving this have been performed by Sweet and Stewart.

CANCER OF THE PROSTATE

Returning now to the prostate gland, all of its enlargements do not fall into the group of hypertrophies; 20% of them are cancerous.

Among Wilson's 468 enlarged prostrates, 73 proved to be carcinomatous—15.5%. Judging from statistics the disease in the past must frequently have been overlooked. According to Thompson, Tanchou found only 5 cases of cancer of the prostate among 8289 patients dead of cancerous disease. Winiwarter noted only one case among 548 cases of cancer in Billroth's clinic. The explanation seems to be simple, the condition escapes detection because of its small extent, and the superficial examinations commonly made. Wilson notes that though enlarged prostates were frequently removed at the clinic, carcinoma was not suspected until microscopic examination revealed a small malignant area.

Hunt found that the disease almost always began in the posterior lobe, from which it is proper to conclude that that portion of the gland should be subjected to the most careful scrutiny in searching for malignant disease.

Secondary carcinoma very rarely occurs, and when found can usually be traced to primary disease of the rectum, bladder, seminal vesicles, penis, or stomach.

It is the primary carcinoma that interests us now. It may assume either the soft, medullary or adenoid form, or be scirrhus, melanotic or mucinoid.

Young and Geraghty describe the gross appearance in these words:

"Carcinoma of the prostate is usually quite characteristic. It is ordinarily hard, tense, and on pressure gives very little sense of elasticity (which is usually not lost even in well advanced fibroid prostatitis.

On cutting into the section it imparts a gritty sensation to the knife-blade, which is absent in the lobulation so characteristic of hypertrophy. Occasionally, where the cancer has invaded a previously adenoid growth, a carcinoma may persist in this tissue, but it is seldom confusing. The finer details of the cut surface vary somewhat; irregularly interlacing bands of varying size are seen, with small, grayish yellow, isolated masses scattered here and there. The interlacing bands are fibrous in character, and the yellowish areas are accumulations of cancer cells. This appearance is not present in fibrous prostatitis, in which the epithelial element frequently disappears, and in which the surface is more smooth and homogeneous than in cancer. Where the cancer is infiltrating in character fine yellow lines can frequently be seen by the aid of a

small magnifying lens. Usually one can be moderately certain of the cancerous nature of the tissue upon gross inspection alone. When the operator's knife, in making capsular incision, cuts through tense tissue that does not bulge, the edges of which are firm and rigid, suspicion should at once be aroused."

FIG. 330.—Osteoplastic carcinomatous invasion of the pelvic bones, secondary to cancer of the prostate. (*Johres.*)

Wilson states that with the possible exception of small tumors of the breast removed at the surgical clinic, carcinoma is in no tissue more apt to escape gross diagnosis than in the prostate, so that it is their inevitable custom to make frozen sections from various areas of the removed gland and report to the surgeon while the operation is in progress.

Wilson and Mc Grath say—

"Microscopically, the adenocarcinomatous tissues present a great variety of arrangements. The acini of the tumor may be small, numerous and grossly crowded together, with compressed cylindrical cells of aberrant type, or they may be large, and loosely filled with aberrant cells containing metachromatic nuclei. In most instances cancer cells infiltrating the stroma are readily demonstrated.

In medullary carcinoma the cells are relatively large, polygonal in type, with a swollen metachromatophilic nucleus. The cells are supported by a delicate capillovascular network.

The scirrhus types show infiltrating lines or groups of aberrant cells, with densely staining nuclei scattered throughout a super-abundant stroma. The stroma itself is frequently infiltrated with small cells containing densely stained nuclei, and is apparently proliferating."

Carcinoma of the prostate in general tends to extend by continuity of tissue to adjacent structures, especially the bladder, the rectum, and the seminal vesicles. Metastasis takes place later to the adjacent lymph nodes, then to the retroperitoneal and inguinal nodes. Metastasis to distant organs is not uncommon, and may be looked for in the lungs, liver, and especially in the bones. There is probably no form of carcinoma that so frequently occasions secondary tumors in the bones, and not infrequently metastasis occurs while the primary tumor is so small as to escape ready observation.

Enlargement of the prostate depending upon the presence of *sarcoma*, is not recognized in adults. It seems only to occur in young children, in whom it is

rapidly fatal. It is usually of the round cell variety, but is so rare that not much is known about it, and some of the reported cases may have been mixed tumors, as they contained striated muscle and other heterologous elements. Growing in the direction of least resistance, these tumors soon reach and invade the wall of the bladder, and extending laterally over the trigone in nodular form obstruct the ureteral orifices, after which hydronephrosis with terminal uremia carries off the little patient.

Tumors of the Bladder

The next group of obstructions affecting the important region of the neck of the bladder results from the presence of tumors of the bladder itself.

The most frequent of these is variously known as the "villous tumor," "villous papilloma," "papillary fibro-epithelioma," and "benign papilloma." Of them, Judd was able to collect 112 cases observed in the Mayo clinic up to 1921. Of a total of 114 cases of vesical tumors, 84 occurred in males and 30 in females. The youngest patient was under 10 years of age, the oldest over 80. The average age was 53.1 years.

These tumors are not peculiar to the bladder, but also, though rarely, occur in the pelvis of the kidney, the ureter, and perhaps in the urethra. An unusually extensive one involving the pelvis of the kidney and upper part of the urethra reported by Judd, is shown in the accompanying illustrations.

The tumor usually occurs in the region of the trigone, but may be situated anywhere. It may be single or multiple, and in the latter event, there may be a large tumor and several small ones. The tumor may consist of a single small group of delicate villi that project upward into the distended bladder or it may be of such extent and magnitude as to cause the greater part of the vesical wall to appear shaggy with complex excrescences. The growth may consist of robust and rounded eminences, some of which are composed of aggregations of villi bound together by mucus and incrusted with urinary salts.

When sections of such tumors are examined microscopically, slightly different appearances may be observed in different cases, though the same fundamental structure is found in all cases. So far as the excrescences are concerned, they all consist of a delicate stalk of fibrillar and vascular tissue, forming a foundation upon which epithelial cells are arranged in superimposed layers—the fundamental structure of papilloma. The cells differ considerably in different cases, rarely appearing like the vesical epithelium from which they are supposed to be derived, but assume a columnar or fusiform shape with the long diameters parallel and perpendicular to the basement membrane.

Between cells which resemble the vesical epithelium and the elongate cells there are intermediate varieties in different tumors. In the cases in which the more normal appearance obtains, the cells are closely attached to one another and to the basement membrane; in those with the distinctly elongate cells, the latter may be very loosely attached to one another or to the basement membrane and the intervals between the villi may be filled with desquamated and entirely loose cells.

From this much examination it is impossible to answer the question always asked by the surgeon—"Is the tumor malignant?" If the surgeon can determine with the aid of his cystoscopic apparatus that the tumor can be made to
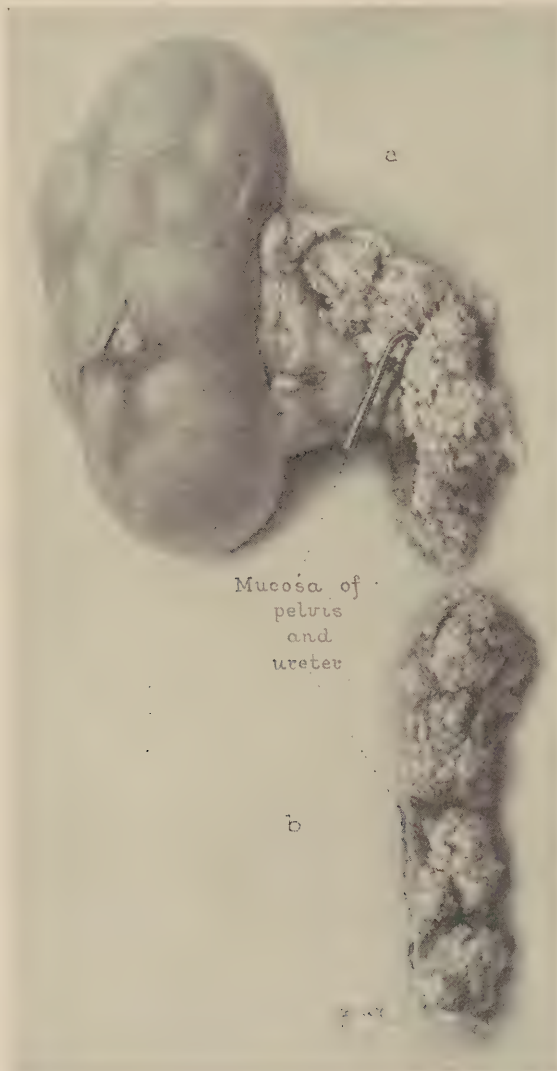
FIG. 331.—Papillary tumor of the pelvis of the kidney. *a*, Kidney with pelvis and upper segment of ureter. The incision has been made in the pelvis and the papillomas forced outward. *b*, Lower end of ureter with multiple papillomas, which probably extend downward into the bladder. (*Judd.*)

move with the mucosa of the bladder wall, it shows that no infiltration has taken place, and that it may be benign; if this cannot be done, the question cannot be answered except by the examination of a portion of the base of the tumor and the discovery of some kind of downward growth. But this is really not neces-

FIG. 332.—Papillary tumor of the pelvis of the kidney.   The open kidney and the exposed
papillomas rising from the mucous membrane of the pelvis.   (*Judd.*)
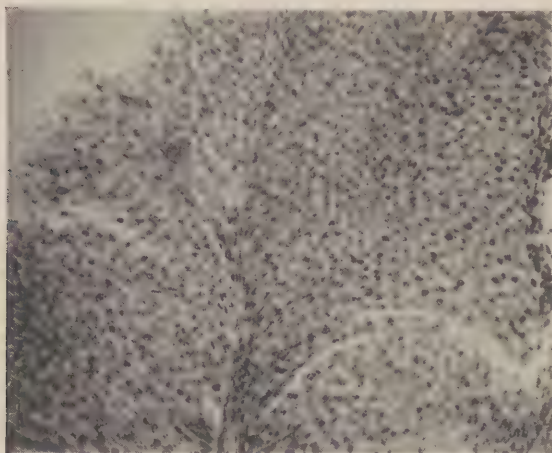
FIG. 333.—Papillary tumor of the pelvis of the kidney.   Photomicrograph of squamous-cell
papillary tumor of the kidney.   The tumor is made up of squamous-cell and slender inter-
vening fibrous stalks.   (*Judd.*)

sary. It is well known that at least 50% of the tumors are malignant regardless of the microscopic findings, and Judd expresses the matter appropriately when he says "from the clinical point of view all papillomas are malignant." He believes that all types of papillomas have the power to recur and to destroy life, and that they would all eventually do so if the patients lived long enough.

But disturbances other than destruction of tissue by local infiltration, and metastasis to distant organs commonly carry off the patient before these are

FIG. 334.—Bladder containing a sessile villous tumor. (*Bowlby and Andrewes.*)

possible. The tumors are commonly so situated as to effect obstruction of the urethral or ureteral orifices, with the resulting train of disastrous symptoms already described as terminating the benign enlargements of the prostate gland. However, in those cases that do have an opportunity to indicate their malignancy through infiltration and metastasis, microscopic examination of the affected vesical wall reveals a microscopic structure analogous to adeno-carcinoma in many cases, instead of the squamous cell carcinoma that would be expected.

The symptoms consist of frequent micturition, with some pain both before and after, burning sensation during urination, hesitancy and retardation of the urinary flow, and above all occasional passage of blood in the urine. Most of these symptoms depend upon the obstruction of the urethral orifice by the tumor, the blood being passed as the result of the trauma effected upon the tumor tissue caught in the neighborhood of the vesical sphincter and compressed. This traumatism not infrequently results in the laceration of the structure, villi of which may be passed with the urine, and the discovery of which is pathognomonic of the condition.

The frequent multiple occurrence of the tumor, and especially in the form of one large and numerous small tumors has suggested that their tissue may be transplantable, and that it is through the engrafting of fragments of the tumor into abrasions of the vesical wall that the multiple tumors occur. Judd calls particular attention to this, and offers in proof the fact that recurrence of these tumors after operation frequently takes the form of a fringe about the urethral orifice.

FIG. 335.—Section of a part of a benign villous papilloma of the bladder. (*Bowlby and Andrewes*.)

When malignant, the tumors may be infiltrative, and occasion metastatis to the regional lymph-nodes, and to the organs, but it is very rare, and the fatal termination usually follows the course of urinary obstruction already indicated.

A more rare form of vesical tumor is the *squamous cell carcinoma*. It also commonly arises in or near the trigone, in the neighborhood of one of the ureteral orifices. Grossly it forms plateau-like elevations of pale color with a tendency to superficial ulceration. Two varieties have been described—a superficial infiltrating, and a deep ulcerating variety. The former extends widely, ulcerates superficially, and does not lead to perforation of the vesical wall; the latter, without such infiltration ulcerates deeply, perforates the wall of the bladder, and invades the perivesical tissue, at the same time that the urine is permitted to extravasate into the cellular tissue.

Microscopically there are also several varieties. Many of the tumors consist of cells that entirely lack any manifestation of the power of keratinization, and so seem to be related to the basal cell tumors; others show a slight degree of keratinization, a few are characterized by a striking amount of it. Not enough comparison of clinical course with pathological findings seems to have been done to enable one to say whether these variations have any clinical significance or not.

The tumors usually effect much dense cicatricial change in the bladder wall, detract from its contractile power, effect closure of one or both of the ureteral
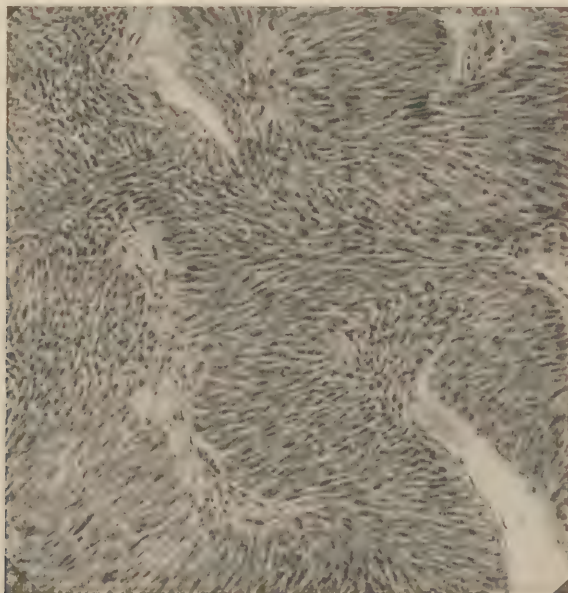
FIG. 336.—Spindle-cell epidermoid carcinoma of bladder. (*Ewing.*)

orifices, occasion unilateral or bilateral hydronephrosis, and commonly occasion death through the train of obstructive symptoms already so often referred to. Metastasis to regional lymph-nodes, and occasionally to the lung or liver takes place, but death is rarely if ever thus caused.

The subject of vesical carcinoma must not be concluded without mention of the very rare occurrence of nodular medullary carcinoma, gelatinous carcinoma, and adeno-carcinoma in the urinary bladder.

Sarcoma of the bladder is rare. Of the 114 primary tumors of the bladder reviewed by Judd, 112 of which were malignant, there was no sarcoma. Bowlby and Andrews, in their "Surgical Pathology," state that carcinoma of the bladder is five times more frequent than sarcoma, in adults. They also quote Targett as stating that the sarcomas occur principally in children under ten and in adults over forty years of age, and that the tumors either occur as "solid sessile tumors projecting into the cavity of the organ, usually from its lower part, or as pericystic growths commencing outside the muscular coat and gradually invading and replacing its walls."

When the case reports are carefully examined, the lack of uniformity in the histological structure of the different sarcomas is striking. Though no great number has been described, they include a surprising number of different varieties—round cell, spindle cell, mixed cell, myxo-sarcoma, rhabdomyo-sarcoma, angio-sarcoma—and some undoubted mixed tumors of sarcomatous nature, in which cartilage and bone have been found. This ascending scale of complexity of structure among such comparatively rare tumors is suspicious, and suggests that the greater number of them may be mixed tumors and have a similar derivation from embryonal material originating through developmental complexity.

Moreover, these vesical sarcomas rarely behave like the simple sarcomas, growing to a large size before metastasis occurs, if it occurs at all.

This, however, may be the result of the anatomical relations of the parts affected, for as can be readily understood, their position may determine that death must result from ureteral obstruction and kidney compression and infection before conditions for metastasis are favorable.

One of the most interesting of the sarcomas of the bladder is a soft polypoid mucinoid growth, usually multiple, and composed of elongated, pedunculated rounded, translucent, grayish polyps, not unlike nasal polyps in general appearance. Microscopically their structure may appear benign and like the edematous fibrillar tissue of the mucous polypi but is more apt to be sufficiently cellular to suggest myxo-sarcoma, on which account they are sometimes described as benign, sometimes as malignant tumors. What the ultimate outcome as regards metastasis might be is uncertain because death usually supervenes from the obstructions effected by their presence. Such tumors almost always occur in young children, and are very probably of the same nature, and perhaps of the same origin as the sarcoma botrioides vaginae of young children.

As rare are certain tumors of which Judd speaks as "non-papillary benign tumors of the bladder." Of these he saw two, and from the literature he was able to collect 30 cases. His cases were described as fibromyomas, and in microscopic structure are said to have been like uterine myomas. Those in the literature are variously described as fibromas, myo-fibromas, and myxo-fibromas.

In closing his section upon tumors of the urinary bladder, Aschoff calls attention to the fact that sarcoma of the bladder seems to be unusually frequent among the workmen in anilin factories, and points out that the well recognized irritative effects of tar derivatives and their resulting tumors, suggests a possible etiological relationship between the two.

The remaining important source of disturbance in the region of the neck of the bladder is calculus.

VESICAL CALCULUS

Vesical calculi are usually single, but may be multiple, and in rare cases great numbers have been found, as in one reported by Birsch-Hirshfeld, in which there were 120 cuboidal phosphatic calculi, having a total weight of 50 grammes, in the bladder of a man afflicted with stricture of the urethra.

Very large single stomes also occur, one reported by Deschamp, having a weight of 1593 grammes, and a circumference of 325 mm.

The calculi seem in many cases to originate higher up in the urinary tract and reach the bladder by descent through the ureter, sometimes without the consciousness of the patient, sometimes with the production of exquisite pain of paroxysmal character—renal colic. But many of them are autochthonous, that is, formed in the bladder primarily, about nuclei that have never been else-where, such as fragments of catheters, hair-pins, bits of ivory and bone, blood clots, collections of tumor cells etc.

The form of the stones varies. Single stones are usually regularly rounded, ovoid or egg shaped. Multiple stones are apt to be flattened upon one or more surfaces, and may be cuboidal.

The structure is usually laminated, different lamina having a different chemi-cal composition, color and density, and representing different chemical condi-tions of crystallization at different periods. The surface and color also vary with the composition. The following types are recognized:

1. *Uratic Calculi.*—These consist of combinations of uric acid with sodium, magnesium or ammonium. They are usually not very large, are of a yellowish brown color, medium density, and have a smooth surface frequently covered with a calcareous surface layer.

2. *Oxalate Calculi.*—According to the older writings the uratic calculi are said to be most frequent, but later writers seem to find those composed of oxalate of calcium to be in the majority. They frequently show admixture of urates, and are not infrequently formed about a nucleus composed entirely of urates. They are dark gray, or if there has been much hemor-rhage as the result of their presence, may be brown black. They are very hard, and the surface is commonly finely nodular like that of a raspberry.

3. *Cystin Calculi.*—These are much more rare, and occur in the so-called cystin diathesis. The stones are usually of small size, rounded form, of a color that varies from white to sulphur yellow, translucent, and of a waxy consistence. Upon section they are laminated.

4. *Xanthine Calculi.*—These are also very rare in comparison with the first two varieties mentioned, and are recognized by rounded form, smooth surface and cinnobar red color.

5. *Carbonate Calculi.*—These are chiefly composed of calcium carbonate, and are recognized by their chalky appearance and fracture.

6. *Phosphatic Calculi.*—According to Aschoff these are to be regarded as secondary calculi, i.e., incrustations upon other and primary calculi resulting from crystallization from abnormal and alkaline urine. However, he admits the possibility of the occasional occurrence of primary calculi of this composition. Many of the phosphatic calculi formerly described, if sectioned will be found to have entirely different internal chemical composition. These calculi are composed of phosphate of ammonium and magnesium, have a dirty white color, crumbly chalk-like consistence, and a rough pumice-stone-like surface.

The calculi are not exclusively composed of the crystalline substance; with it there must be a binding substance, which is usually mucus from the urinary passages. Wells, in his "Chemical Pathology" gives the following explanation of the formation of the stones: "Although the amount of colloidal material in urine is relatively small, yet it undoubtedly plays an important part in main-taining in solution the less soluble crystalloids, which are especially the urates and calcium oxalate. Normal urine contains no colloids which form irreversible gels, and hence ordinary deposits can be readily dissolved, but in inflammatory conditions there appears fibrinogen which readily forms the irreversible fibrin, and conditions thus become favorable for the formation of concretions of any crystalloid with which the urine may be saturated or over-saturated at the time."

Shattuck has shown that in uratic calculi (uric acid calculi) the presence of cells or other organic matter as a nucleus, is very rare, the center being almost always a primary crystalline deposit from a super-saturated solution.

But when the calculus results from the deposit of a salt upon some primary calculus or upon a foreign body by which inflammation has been caused, it is most apt to consist of ammonio-magnesic phosphate and ammonium urate.

Vesical calculi rarely occur without exciting cystitis, or inflammation of the bladder, and as Ribbert is careful to point out, an interesting vicious circle is at once established, for the stone provokes cystitis and the latter favors the growth of the stone. At first the inflammation of the bladder wall is catarrhal, but in the course of time it is almost sure to become ulcerative, not as is frequently stated through the weight of the stone and the pressure it exerts, but through the protection it affords the micro-organisms causing the inflammation by interfering with the free evacuation of the bladder and the escape of the infected urine. If the first idea were correct, the larger the stone, the greater must be the ulceration. Such is not the case. Some very large stones, of relatively great weight are almost without ulcerations, some relatively small ones are associated with large and deep ones.

Not only does the stone thus predispose to ulceration after infection, but it obstructs the urethral entrance and makes micturition difficult, increases the work of the bladder and causes it to hypertrophy, and predisposes to diverticulum formation, and obstruction of the ureteral orifices. It thus again becomes a cause of the symptom-complex, that eventuates in hydronephrosis and uremia. But these results arrive late in vesical calculus, and many cases go for years without them, the danger of the ascent of the infection to the kidney and the destruction of patient through pyelo-nephritis being far greater.

Renal Calculus

Many of the stones that occur in the bladder are first formed in a higher part of the urinary tract from which they descend. Most of them originate in the pelvis of the kidney, where they form in the recesses of the calyces. Most of them consist of uric acid. It is quite frequent for a fine crystalline deposit to be passed with the urine, in the form known as "gravel," and it may be in the occurrence and retention of some of this that the larger formations originate. It has been argued that for the formation of the calculus, associated or antecedent inflammation is essential. That seems to be an error. Careful examination of the mucous membrane of the pelvis of kidneys in which small stones were present, entirely failed to discover the expected disturbance.

Calculi formed in the renal pelvis may remain there, and receiving continuous accretions of uric acid, increase in size to a remarkable degree, at times filling the entire pelvis, and extending into the calyces between the pyramids in a branched or coral-like form. Under these circumstances the pelvis may be so filled that the free passage of the urine is prevented and a local hydronephrosis is effected, the calculus even growing larger as the space to contain it increases. Usually there is but one stone, but there may be several, and when they are in contact, the approximated surfaces may be facetted as though from friction.

Not only do the stones occasion the dilatations described, but they also predispose to infection, ulceration, and destruction of tissue as in the bladder, and may bring about the death of the patient through purulent infiltration of the kidney.

In all probability but few of the stones that form in the renal pelves remain there. Most of them pass down the ureter. As has been said, if they are small and the passages open, this may be a simple matter that takes place without the knowledge of the patient, but if the stone be a little larger at the time its migra-

Calices contain pieces broken from large stone

FIG 337.—Coral shaped calculus in the hydronephrotic renal pelvis. (*C. H. Mayo.*)

tion begins, or if the passages be narrow, it may be slow and painful. The character of the parozysmal pain is intense, and such that the most courageous cannot endure it without a groan. In most of the text-books the pain is said to be the result of the traumatic injury effected by the calculus as the peristaltic movements of the muscles of the ureter drive it on, and the blood that frequently stains the urine at the time, to depend upon the laceration of the mucosa of the ureter. But the pain is largely due to the temporary plugging of the ureter by the calculus, and the backward pressure of the urine, accumulating behind it, upon the kidney. If it were not so, how could exactly the same symptom result from the kinking of the ureter in floating kidney with "Dietl's

crisis?   There is no calculus and no traumatism in that condition, yet the pain is the same, and in rare cases the urine may be bloody.

The most difficult part of the ureter for the stones to pass seems to be the lower extremity where the tube passes through the wall of the bladder, and there they sometimes remain, unable to escape.   In such cases although the stones cannot get out, the urine seems to get by, and we have seen a case in which four small calculi occupied a local dilatation of the ureter in the wall of the bladder, without great dilatation of the ureter above them, and with only slight hydronephrosis.

Fig. 338.—Calculus detained at the orifice of a ureter, seen through the cystoscope.   (*Louis and Mark.*)

No doubt most of the calculi that succeed in passing through the ureter also succeed in passing through the urethra and escaping from the body altogether. It is only occasional calculi that remain in the bladder and form the nuclei of the larger vesical calculi.   Occasional stones that enter the urethra fail to leave it, but are detained in the fossa navicularis where they increase in size through accretion, and in the course of time may become the size of date stones or even much larger, occasioning great interference with the escape of the urine during the act of micturition.

Hydronephrosis

In all of these obstructive conditions, mention has been made of the dilatation of the urethers, the enlargement and excavation of the hila of the kidneys with atrophy of the renal substance, and the frequent destruction that follows ascending infection of the kidney.

The possible mechanism of hydronephrosis has also been considered, but the morbid appearances have not been described.

If a ureter, as sometimes happens, be included in a ligature and completely and permanently closed, the kidney for sometime thereafter continues its function, and the secreted urine, unable to escape, collects and distends the

Fig. 339.—Infected hydronephrosis with multiple nephrolithiasis.   (*C. H. Mayo.*)

ureter and pelvis, stretching their tissues and thinning them.   This is an *acute hydronephrosis*, and is of brief duration, because when a certain quantity of urine has been secreted, and the backward pressure has reached a certain point, secretion stops, atrophy of the organ begins, and much of the water of the already secreted and retained urine is absorbed.   From this it is learned that true hydronephrosis is always chronic and depends upon incomplete obstruction of ureters which are gradually and progressively dilated.

In the various chronic obstructions above referred to—those from enlarged prostate, tumors about the uretheral or ureteral orifices, vesical calculus, stric-

ture of the urethra, etc.—there is usually intermittent rather than continuous obstruction. During the vesical contraction attending urination, the ureteral orifices always normally close, but when the bladder hypertrophies, the muscle bundles may be so abnormally disposed as to keep them partially closed all the

FIG. 340.—Dilatation of the ureters and hydronephrosis from long-standing prostatic enlargement with obstruction. (*Deaver.*)

time, and prevent them from completely closing at any time. The inevitable result is that the peristaltic movements of the ureters must be increased in order that the tubes discharge their contents. Such increased muscular activity is

followed by hypertrophy of the ureters, the walls of which thicken in proportion to the work they have to do until the physiological limit of increase is reached.

The ureters thus are transformed into thick walled structures, the diameter of which may equal that of the small intestine, and instead of being straight and of uniform calibre, they may be tortuous, kinked and sacculated.

With extreme dilatation the primary thickening of the wall gives place to secondary thinning as the muscular tissue is obliged to yield. The distension of the pelvis of the kidney enlarges its hilus, and bends the substance of the kidney outward at the same time that the calyces are distended and the pyramids flattened. Continuance of these displacements plus the compression of the kidney substance by the retained fluid, is followed by atrophy of the parenchymatous tissue, beginning in the collecting tubules, and extending upward into the cortex, which slowly becomes transformed into a kind of thin rind that in extreme cases seems to be composed chiefly of connective tissue, but in which more or less numerous glomerules can always be found.

Hydronephrosis is usually bilateral, and the destruction of the kidneys determines the death of the patient before the enormous size occasionally seen in unilateral disturbance is possible. If the hydronephrosis be on one side only, and the other kidney undisturbed, so that the urinary secretion is possible, there is no reason that the patient should not live indefinitely, and the distension progressively increase.

Through the kindness of Dr. George W. Perkins there came into the hands of the writer a number of years ago, an ovoid tumor larger than a cocoanut, shaggy from adhesions upon the external surface, dark in color, so hard that it could not be cut with a knife, and partly filled with fluid as was indicated by a succussion shock when it was shaken. It had been removed from the abdomen of a man run over by the wheel of a wagon, and who had made a good recovery after a long period in the hospital. Some years after the accident, he returned with symptoms of an abdominal tumor, and the specimen had been removed. With the aid of a saw the mass was opened and examined, and proved to be the relics of an enormously hydronephrotic kidney, reduced to a very thin walled sac, the interior of which was thickly incrusted with uratic and phosphatic salts.

SURGICAL KIDNEY

If the contents of the partially obstructed ureter become infected, and purulent in consequence, the condition becomes transformed into what might with justification be described as *pyo-nephrosis*. It is soon followed by infection of the kidney from its pelvis, the resulting condition being commonly described as *pyelonephritis*. As has already been pointed out, there are two entirely different conceptions of the path by which the infectious agents reach the kidney. Nearly all of the text-books of pathology explain it is an ascending infection, that is, one that ascends from the bladder to the ureter, from the ureter to the pelvis of the kidney, and from its pelvis, into the tubules of the kidney directly in the detained urine. But, as has been shown, this is subject to the doubt thrown upon it through inability to reproduce it experimentally, and has there-

fore, in the thought of many given place to the idea that it is indirectly, and by transportation through the lymphatics, that the infectious agent reaches the kidney. However that may be, the result is what is frequently called "surgical kidney," probably because it is the result of neglected surgical conditions, and is an acute pyogenic inflammation of the organ.

Purulent nephritis, in more rare instances may be caused through the presence of micro-organisms brought to the kidney by the blood, from malignant

FIG. 341.—Pyelonephritis—case of prostatic obstruction with cystitis. (*MacCallum. "Text-book of Pathology."*)

endo-cardial lesions, from infected wounds with pyemia, etc. Under such circumstances it is always bilateral, and the primary disturbances seem to be more frequently in the cortex. In the ascending infection, the disturbance may be unilateral, and seems first to occur in the medulla. In most cases the discovery of obstructive disease of the lower urinary passages—enlargement of the prostate, stricture of the bladder, stone in the bladder, tumors at the vesical outlet, etc., etc., are sufficient to enable one to decide that the infection ascended to the kidney from below. From an examination of the kidney alone, it may be impossible to tell the origin of the disturbance. Really both varieties look very much alike.

In the ascending variety, with which we are here concerned, the suppura ton seems to begin in the medulla, and there the lesions are certainly most distinct and most advanced. Supposedly the bacteria enter the kidney through the mouths of its collecting tubes or ducts, in which they grow, ascending towards

the cortex. As the bacteria increase in number, they partly or completely fill the invaded tubules, and may form cylindrical masses equal in size to the lumen —bacterial tube-casts. These masses of micro-organisms soon effect the death of the epithelial cells which line the tubule, and then find their way into the interstitial substance of the kidney. As this is in progress, leucocytes cluster in and about the bacterial masses, and abscesses form, at first small, then larger, and then, through coalescence, still larger until eventually the greater part of the cortex may be destroyed. Upon section of such a kidney, the pyramids of the medulla appear striated by broad lines of yellow, which are the lines of suppuration. In some cases hemorrhage about the areas causes them to be surrounded by dark red zones. As the medulla becomes destroyed, the ascent of the infection to the cortex begins its destruction, and when the extent of the invasion is such that adequate secretion of urine becomes impossible, death must follow. Before this, and especially in unilateral cases, the cortex is sometimes penetrated, and a little of the pus containing the micro-organisms escapes into the peri-renal cellular tissue, with resulting more wide-spread suppuration and the occurrence of *peri-renal abscess*.

FIG. 342.—Tuberculous pyelonephritis. (*Stengel and Fox, "A Text-book of Pathology," modified from Bollinger*.)

When the outer surface of such an infected and suppurating kidney is examined with the naked eye, it appears mottled, and when a longitudinal section is made, and the edge of the capsule seized and stripped from the organ, it is found to peal off very easily on account of the edema associated with the inflammation, leaving a smooth surface with numerous small yellow or red eminences of more or less rounded form, which are the swellings corresponding to the upward terminations of the lines of infection extending from the medulla outward to the cortex. It is through opening and outward evacuation of one or some of these that the peri-nephritic abscesses are formed.

In some cases the condition is not fatal, and recovery ensues after destruction of the micro-organisms, absorption of the exudate, and the formation of cicatricial tissue. Occasional of the abscesses become encapsulated and the unabsorbed contents calcify. The surfaces of such kidneys usually show dense scars where the abscesses have been. Calcified areas formed as described are commonly mistaken for old tubercles.

The pyelonephritis that results from the presence of a calculus in the pelvis of the kidney, without any obstructive disease below, cannot be imagined to result from ascending infection. It must depend upon micro-organisms brought to the kidney by the blood and in process of elimination. No doubt many micro-organisms are continually thus being eliminated from the body without injury to the kidney structure because of their small numbers and because of the good resisting power of the healthy renal tissues. But if a stone in the pelvis of the organ alter these conditions by presenting opportunity for the organisms to collect locally and multiply, at the same time that the tissues are diminished in vitality and their interspaces opened by traumatic injury, conditions are notably altered, and infection takes place.

DISEASES OF THE TESTIS AND EPIDIDYMIS

ORCHITIS: EPIDIDYMITIS

Enlargement of the testis may be either acute or chronic. The former may follow injury. More frequently it occurs as a complication of acute infectious disease, notably in mumps, less so in typhoid fever, the infectious agents reaching the organ by metastasis through the blood. Its most common cause is gonorrhoea, the cocci presumably finding their way along the urethra, through the ejaculatory ducts into the vas deferens, thence into the epididymis and finally to the testis.

In the hematogenous infections it is the testis itself that suffers, in gonorrhoea, chiefly the epididymis. In the former the swelling is moderate and painful because of the inelasticity of the tunica albuginea testis, in the latter, considerable, the increase beginning in the globus minor, extending to the globus major and affecting the testis only moderately.

Because of its inability to swell, inflammation of the testis is not only very painful, but may result in atrophy and destruction of spermatogenesis. Fortunately the condition is usually unilateral. Testicular atrophy is sometimes followed by hypertrophy of the mamma of the affected side.

Except the rare cases which follow external traumatism, and are accompanied by an external wound, acute orchitis almost never progresses to suppuration. It is characterized by congestion, more or less round cell infiltration, and slight hemorrhage, and recovers by resolution with more or less diffuse fibrosis, the contraction following which is responsible for the subsequent atrophy.

Of far greater importance from the surgical point of view are the chronic enlargements of the testis. These result from tuberculosis, syphilis and tumors.

TUBERCULOSIS OF THE TESTIS

It is rare for uro-genital tuberculosis to make its appearance independently of tuberculous disease in other organs, notably the lungs.

The disease not infrequently follows traumatism without external injury, which made it mysterious until it was discovered that tubercle bacilli are occasionally present in the seminal tubules of apparently normal testes, to which they

are presumably transported, by the blood, from the pulmonary lesions, and in which they remain inactive until afforded an opportunity for multiplication and invasion. Tubercle bacilli have been found in undescended testes.

Urogenital tuberculosis in the male, usually begins in the epididymis, from which it extends to the vas deferens, seminal vesicles, prostate, bladder, ureters and kidneys. There is usually, however, some disease of the testis itself, and remembering that the bacilli have sometimes been found in the seminal tubules of testes that show no disease, it is possible that the testis supplies the bacilli that escape from its tubules to infect the more susceptible epididymis.

The disease appears and makes most rapid progress in the tail or globus minor. The whole of the epididymis soon becomes affected, and greatly enlarged and nodular, appears "like a thick sausage studded with caseous nodules, attached to the testis which itself shows only a few little nodules in the corpus of Highmore and here and there in the parenchyma" (Kauffmann).

The enlargement may be associated with vaginalitis and more or less hydrocele. But as the head of the epididymis, where there is no tunica vaginalis testis, soon shows the greatest extent of disease, such exudation usually accompanies those cases in which the tail of the epididymis and the testis itself are exceptionally affected. If the inflammation of the membranes be limited in extent, and unaccompanied by serous exudation, adhesions may form, beginning at the posterior surface, and extending anteriorly.

FIG. 343.—Tuberculosis of the epididymis (longitudinal section). The epididymis is filled with cheesy nodules. In the upper right portion the disease can be seen invading the testis. In the central portion of the latter is a white cicatrix. (*Aschoff*.)

The disease is usually first discovered by the patient as a nodule either at the tail or head of the epididymis. There is little pain, and enlargement is slow. If the organ be removed and examined, at this early period, the lump is found to consist of a solid or semisolid caseous mass, of a slightly yellowish color, varying in softness from Rochfort cheese to thick cream. If the disease be more advanced, there may be many such areas, some circumscribed, some coalescent, some situated in the substance of the epididymis, some upon its surface, some ascending along the spermatic cord, with occasional small ones in the neighborhood of the rete testis, or more deeply in its substance.

If no surgical intervention be practiced, and the disease progress to its most destructive form, extension to the adjacent soft tissues of the scrotum, brings it to the surface, where the softened caseous contents may evacuate through fistulas from which granulation tissue may later fungate.

Microscopical examination usually reveals typical tubercles. The disturbance seems to begin with the accumulation in a tubule or a system of tubules, of the epididymis, of a yellowish creamy, translucent material composed of desquamated and degenerated epithelial cells, leucocytes and fat molecules, with numerous tubercle bacilli. Presumably the bacilli, first effect catarrhal inflammation with desquamation of the epithelial cells, by which they are admitted
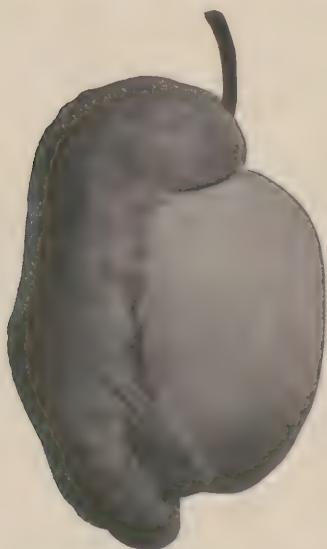
FIG. 344.—Tuberculosis of the epididymis, showing the sausage-like swelling surrounding the testis on the left. (*Aschoff*.)
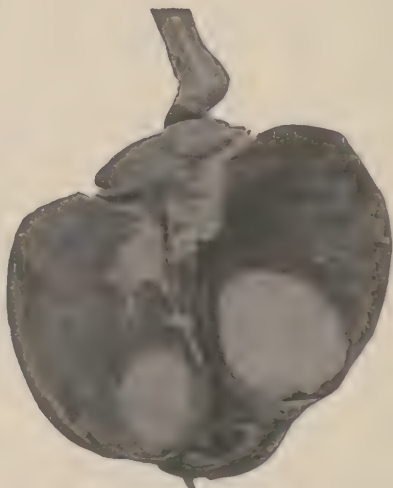
FIG. 345.—Tuberculosis of the testis. An isolated caseous nodule in the testis without disturbance of the epididymis. (*Aschoff*.)

to the interstitial tissue to form in succession miliary tubercles, conglomerate tubercles, and large tuberculous masses with necrotic centers and softened contents whose evacuation through the vas deferens transforms them into cavities, at the same time that the infectious agents are carried to the higher parts of the uro-genital tract.

The disease is commonly bilateral. It has been observed in infants only a few months old, and in men of 75 years. It runs a variable course. In many cases ascending infection of the uro-genital tract follows quickly; in others the disease long remains localized. In the latter case it may be highly destructive, large tuberculous lesions undergoing extensive caseation, giving rise to considerable excavations that open with permanent external fistulas, or, opening into the cavity of the tunica vaginalis testis, occasion purulent vaginalitis which may later open through external fistulas. In the most favorable cases the progress of the disease is slow and the lesions tend to cicatrize and calcify.

As has been said, the invasion of the testis is usually very slight, and characterized by the appearance in the corpus of Highmore and the mediastinum testis, of scattered grayish more or less discrete or confluent miliary tubercles. In occasional cases the testis may be more extensively involved, but there is

usually little of the softening and excavation that characterizes disease of the epididymis.

Testes removed at autopsy occasionally show tuberculosis of another form and without disease of the epididymis. Both testes are usually similarly affected, the condition being secondary. The lesions, arise in the interstitial tissue, in the form of a smaller or larger number of miliary tubercles, which gradually surround and include adjacent tubules, which are destroyed. So long as the lesions remain frank miliary tubercles there is no difficulty in recognizing them. But if they attain to a considerable size and effect the transformation of the tissue into grayish homogeneous necrotic masses, the question frequently arises whether they are not syphilitic. It might be supposed that this question could easily be answered by a histologic and bacterioscopic examination, but that is not the case. The discovery of the relative specific micro-organisms, is conclusive. In its absence the general resemblance between the lesions of tuberculosis and syphilis is confusing.

Orth laid stress upon the more rapid destruction of the elastica by the tuberculous disease, and supposed that if delicate circles of elastic tissue were still visible in the necrotic area, it was in favor of syphilis. Baumgarten believed the presence of the giant cells of Langhans to be sufficient to stamp the lesion as tuberculous. The former is probably the more useful character as there may be no giant cells in tuberculous lesions, and they may be present in syphilis.

Following tuberculosis of other organs, and probably as the result of the dissemination of toxic substances through the blood, the testis sometimes suffers from fibrosis and atrophy. E. Fraenkel observed this condition, and to it gave the name *Spermatoangitis fibrosa obliterans*.

SYPHILIS OF THE TESTIS

This assumes two forms, *fibrous orchitis*, and *gummatous orchitis*. In the former the organ becomes atrophic, smaller than normal and abnormally firm; in the latter larger than normal and sometimes very soft.

In syphilitic disease it is the testis itself that is affected in nearly all cases; in tuberculosis it is the epididymis that first and chiefly shows the lesions.

Moreover, the testis in syphilis, even though it may be enlarged to the size of a goose egg, and largely destroyed through gummatous softening, is painless.

With a history of antecedent syphilitic infection, and a positive Wassermann reaction on the part of the patient's blood, a slowly developing painless enlargement of the testis itself, should offer no difficulty in diagnosis.

Under antisyphilitic treatment, the lesion tends to recover as rapidly and as completely as the extent of destruction permits.

When a gummatous testis is examined, it presents a somewhat variable appearance, according to the extent and type of disease. It is enlarged to an extent that may reach the size of a goose egg; it is usually hard, and upon section appears fleshy, pale red, grayish or whitish in color, either soft or hard and cicatricial in consistency. Its substance is usually beset with projecting rounded or irregular hard nodes of pea or bean size. These are usually dry, structureless, opaque, reddish, yellowish or grayish in color. Gummas of different age differ

in appearances and consistency. If old, they may be yellowish and soft from necrosis, and may be surrounded by a connective tissue capsule that is thick and tough. Some testes are cicatricial and without the definite gummas, others show numbers of miliary gummas in the cicatricial tissue, others contain large and distinct gummas.

The general tendency seems to be towards final cicatrization, but a certain number soften, perforate, and discharge the gummy contents externally. In such cases fungating granulation tissue may appear externally.

Untreated cases that do not evacuate, run a course of variable length, the softened areas disappearing by absorption, and leaving the testis much diminished in size, and very hard from fibrosis. Delayed absorption not infrequently results in calcification of the necrotic areas.

When the tissues are examined microscopically, varied appearances are presented. The disturbance appears to begin with the formation of a cellular granulation tissue that arises between the seminiferous tubules, pushing them apart, compressing them, and including a greater and greater number of them, as it extends. As the lesion progresses, some of this tissue advances to fibre formation, thus giving rise to the dense cicatricial areas, while the remainder undergoes necrosis.

Fig. 346.—Syphilis of the testis (longitudinal section). The testicular tissue is completely transformed into cicatricial fibrillar new formation in which are several circumscribed gummas. (*Aschoff*.)

The recognition of the lesion as syphilitic is sometimes fraught with difficulty. The salient features are as follows: first, the discovery of the specific microorganism by the specific method of staining; second the presence of an unusual number of plasma cells in the exudate; third, the discovery of the vestiges of the elastic tissue by which the tubules were originally surrounded, which remain visible for a long time after their cells have disappeared.

The granulation tissue is well vascularized, but the larger vessels may show syphilitic endarteritis. Small gummas may appear strikingly similar to miliary tubercles, and may contain Langhans giant cells, so that they are of no value in differentiation.

TUMORS OF THE TESTIS

As tumors of the testis rarely affect the epididymis, there ought to be very little danger of confounding them with tuberculosis. But as they occur as

growing enlargements—as compared with the inflammatory lesions—and are usually painless at first, there may be some danger of confusing them with syphilis. Immediate recourse should be had to the history of the case and the Wassermann reaction.

Most of the tumors begin about the hilum of the organ, and extend forward, pushing the tissue aside in such manner that it eventually forms a kind of partial
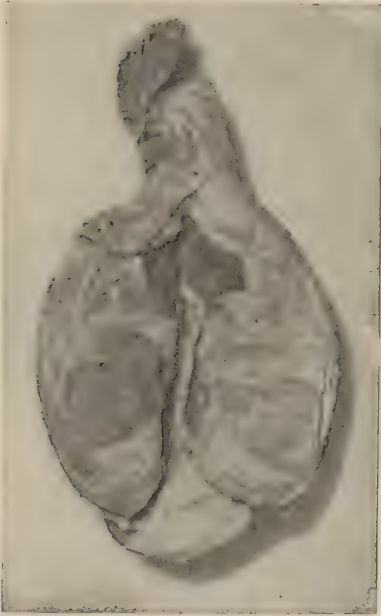
FIG. 347.—Gumma of testicle. The firm caseous nodules are surrounded by scar tissue. (*MacCallum* "*Text-book of Pathology.*")
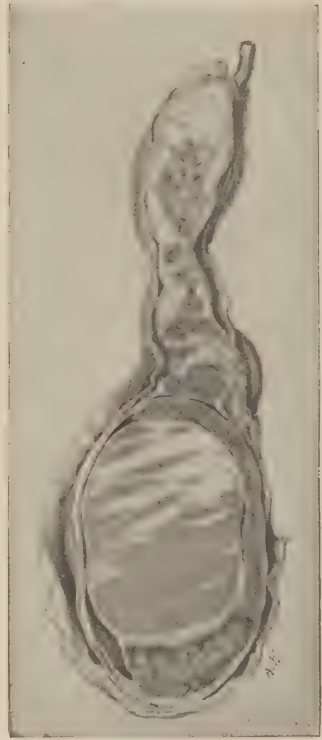
FIG. 348.—Syphilitic fibrous orchitis. (*MacCallum*, "*Text book of Pathology.*")

covering for the new growth. Usually there is a single node that does not greatly alter the rounded oval form of the testis. A few of the tumors pervade the tissues of the testis instead of displacing them.

With the exception of the ovary, there is probably no organ whose tumors are so difficult to subject to satisfactory classification. A few are histologically simple and can be assigned to well recognized classes; the greater number are highly complex and many are unclassifiable.

This is partly because of the frequency with which teratomas and mixed tumors occur in the sex glands, partly because of the peculiar specialized tissues of the sex glands, many of whose cells though derived from the mesoderm, have the morphology of epithelium.

It is doubtful whether there are many simple tissue tumors of the testis. *Fibromas* have been described as occurring in the tunica albuginea, or arising from the rete testis. *Lipomas* have been found in the tissues of the spermatic

cord. In the older books one can find case reports of *chondromas* and *myomas* originally regarded as simple tumors, but added acquaintance with them arouses the suspicion that they were mixed tumors with preponderance of the respective tissues after which they were called.

The scientific aspects of the mixed tumors and teratomas have been given at considerable length in the part of this work that treats of the "Congenital Conditions of Surgical Interest," and further discussed in the section devoted to Tumors, so that it is unnecessary to repeat them here. It will be assumed at this point that almost all of the tumors of the testes are of the mixed variety, and as such may have structure relatively simple or complex according to circumstances, and may be relatively benign or malignant, according to the histological structure they present. Upon this basis it will also be assumed that they are all potentially, and most of them actively malignant, and therefore proper objects for surgical intervention and removal.

The tumors, however, manifest themselves differently, clinically. Some appear during childhood, and grow rapidly; others not until long after middle life. Some appear for no known reason, others seem to arise as the result of traumatic injury. These are, however, but peculiarities shared by tumors in general.

Most of the tumors that appear before the 40th year, grow rapidly, have a highly cellular structure, quickly extend to other viscera, and prove fatal sometimes within a few months, others most commonly developing after the 40th year, grow relatively slowly, invade the adjacent tissues of the scrotum, slowly extend through the lymphatics, and later occasion death through destruction of the internal organs. Both tend to recur again and again if excised. The former seem to bear a general correspondence to the sarcomas, and are commonly so called; the latter, rather resemble the carcinomas, and most commonly meet with that designation.

As a means of approach to the study of the tumors, this clinical classification may be momentarily adopted.

Sarcoma of the Testis

The tumors called by this name, as has been said, usually occur before the 40th year of life and may be unilateral or bilateral. They may present themselves as fairly well circumscribed nodes by whose growth the substance of the testis is displaced, or they may infiltrate the entire substance of the organ, including the epididymis, transforming it into a great mass of miscellaneous tissues.

In some cases the tumor seems to be composed entirely of spindle cells sometimes smaller, sometimes larger, corresponding to spindle cell sarcoma as it appears in other organs, and behaving in much the same way. In others there are broad and narrow strands of spindle cells that traverse the tissue of the more or less disturbed but still recognizable organ, separated from one another either by the proper tissue of the testis, of by a delicate granulation tissue, parts of which are edematous if not mucoid. These are the spindle cell sarcomas.

In other cases, usually of more or less diffused tumors, the structure is chiefly composed of round cells. Bowlby and Andrewes state that the round

cell tumors are usually composed of large round cells, which immediately stamps them as more or less nondescript. The cells are not infrequently regularly arranged about the blood-vessels, and such tumors are commonly called perithelial round cell sarcomas. It was perhaps them that Krompecher had in mind when he expressed the opinion that most of the tumors of the testis were derived from the endothelium, especially of the lymph vessels.

The spindle cell sarcomas are usually small, and relatively hard and dense; the round cell sarcomas large soft tumors. The cut surface of the former is fairly uniform, that of the latter is apt to be variegated by alternating areas of necrosis, hemorrhage, testicular tissue, and healthy tissue of the tumor. The latter also grow to a far greater size, not infrequently becoming as large as a goose egg and sometimes embrace the epididymis and spermatic cord.

Both tumors early invade the pelvic and then the retroperitoneal lymph nodes, and both also distribute their cells by way of the blood, effecting metastatic colonizations in distant organs, from the effects of which the patient usually dies.

Carcinoma of the Testis

These tumors appear after the 40th year of life, and are usually unilateral. In very rare cases described as scirrhus cancers, they grow slowly, are hard, remain small and soon effect adhesions between the testis and the scrotum into which the tumor infiltrates reaching the surface which ulcerates, and fungates as in cancer of the breast.

But in nearly all cases the testis increases to a considerable size without adhesion and infiltration, and without material alteration in shape. There may be much pain as the tunica albuginea is stretched, and in many cases, of the similarly growing sarcoma as well as of this so-called carcinoma, the membrane may eventually rupture, permitting blood to escape into its cavity. Bloody fluid in the tunica vaginalis testis in cases where there has been no traumatism, is hence, highly characteristic of malignant disease of the testis. The disease soon distributes its cells through the lymphatics to the pelvic and retroperitoneal lymph nodes, which sometimes reach a very large size, and later to the organs which they may destroy.

When these tumors are examined microscopically, they are found to be partly composed of large cells of undoubtedly epithelial appearance. In the so-called scirrhus tumors, they are of more or less rounded form, and arranged in nests or alveoli as in ordinary cancer. In the large soft variety the appearances differ in different cases. In some there are large nests of rounded cells, supposed to be descended from the undifferentiated spermatogonia arranged about fibrovascular axes, and to such tumors the name *seminoma* is frequently applied, especially by French writers. In other cases the cells are definitely columnar in shape, giving the tumor much the appearance of the columnar cell carcinoma—*adeno-carcinoma*.

It is certainly possible that each of the structures described represents a distinct entity, and a definite type of tumor, but doubt upon the correctness of such an assumption is aroused when it is found that the tumors appear like

sarcoma in some parts, and like carcinoma in others, and that it is common to find areas of mucoid, muscular or cartilaginous tissue in the stroma of either. That at once stamps the tumors in which it is found as "mixed tumors," either sarcomas or carcinomas, or neither—as the pathologist concludes.

There is also doubt as to the so-called *adenoma* of the testis. It is occasionally seen in children and adults, and not only in perfectly developed organs, but also in those that have failed to descend, and in hermaphrodites. They make their appearance as single or multiple, rounded, well circumscribed nodules, imbedded in the testicular substance, and microscopically composed of tubules much like those normal to the organ and supposed to develop from the cells of Sertoli. They are so rare that little is known about them, but it is possible that they have some relation to the *Cystadenomas*, which are more commonly large, well circumscribed tumors, sometimes observed in children, but more frequently in adults, composed of fibro-connective tissue, riddled with epithelial lined spaces many of which have undergone cystic dilatation through accumulation of mucilaginous fluid. Some of the tubules are lined with ciliated epithelium, occasional others with squamous cells. When such tumors are studied with reference to the stroma, they are commonly found to contain smooth or striated muscle or cartilage. If they show derivatives from all three blastodermic layers they are embryomas; if of only two, they are mixed tumors. So long as the tumors having these structures remain circumscribed, their nature may be determined. But how shall the nature of a teratoid tumor or a mixed tumor be determined if its connective tissue shows sarcomatous growth or its epithelial tissue carcinomatous growth, and the composite structure is masked by the disproportionate and riotous growth of its malignant components?

It may not be possible to say how a tumor of the testis began, or to determine accurately what it is. The separation into sarcomas and carcinomas is clinical not pathological, and the pathologist can call the tumor what he pleases without serious danger of contradiction.

DISEASES OF THE UTERUS

The material removed by the curet—uterine scrapings—is amongst that most frequently received in a laboratory, and therefore that from which the surgical pathologist is very commonly called upon to make a diagnosis.

In most cases nothing more is asked than an expression as to the malignancy or benignancy of the condition of the diseased uterus. Fortunately, in the majority of cases this presents little difficulty, and in all probability the greater number of diagnoses are correct. But in a certain proportion of cases the appearances of the normal uterine mucosa are peculiar, and the state of the endometrial cells such as to occasion grave doubts in the minds of the inexperienced, who may readily fall into the error of "giving the patient the benefit of the doubt" and expressing the opinion that what he sees is a sign of "beginning malignant disease," with the unfortunate result that the patient may be persuaded to undergo an operation attended with danger, and mutilation.

To avoid such error it is important to remember that there are a number of normal variations in the endometrium. For convenience of description these may be divided into those that are chronologic, those that are topographic, and those that are physiologic.

Before taking these up individually, however, it is necessary to recall that the uterine mucosa, or endometrium, consists of an epithelial surface covering from which simple and bifurcated tubules descend into a supporting corium or stroma. The latter consists of a peculiar and characteristic structure fairly well corresponding to what is ordinarily described as a lymph-adenoid tissue. It is sharply separated from the muscular substance of the myometrium, but not by a straight line, for its dips into the spaces between the muscular bundles for a short distance, so that its lower surface forms a wavy line, and here and there it follows the blood vessels to an unusual depth. A considerable part of it consists of a delicate reticulum of branching cells like those of embryonal connective tissue, in the meshes of which lie great numbers of round and spindle cells, the former being more numerous except about the glands and blood vessels where the spindle cells preponderate. Both varieties of cells have deeply staining nuclei and so little cytoplasm that ordinarily it is not seen. Occasional capillary blood-vessels course through the stroma.

I. *Chronological Variations in the Endometrium.*—In childhood and old age, meaning by these terms the periods preceeding and succeeding that of reproductive life, the general appearances of the endometrium are much the same except that in the former it is more cellular and in the latter more fibrillar. It is thin, its glands are few in number, and they frequently run diagonally instead of directly down. The surface epithelial cells are either low columnar or cuboidal in form, and are quite regularly without cilia.

In very old women there may be areas in which the cells approach the squamous type. Some of the glands may be cystically dilated.

During the reproductive period the epithelium is more uniform, more regularly ciliated, the glands larger and more numerous, and the stroma much thicker, but during this time the other factors come into play to modify its appearance.

II. *Topographical Variations in the Endometrium.*—During the reproductive period of life, the endometrium lining the corpus uteri consists of a surface covering composed of cuboidal or low columnar cells most of which are provided with cilia whose lashing movements are outward. Each is provided with a nucleus of relatively large size, situated in the center or below it according as the cells are cuboidal or elongate: it is distinctly vesicular and fairly rich in chromatin. The cytoplasm of the cells is fairly clear, and is slightly basophilic in staining reaction.

At the isthmus the cells begin to become more definitely columnar and elongated as they descend, until at the cervix they are high columnar cells with elongated nuclei situated low down toward the basement membrane. Most of these cells are definitely ciliated. Their cytoplasm is usually quite clear, and gives a basic reaction.

The glands descend perpendicularly into the stroma, and are numerous, simple or bifurcated tubules lined with definitely columnar ciliated epithelium.

Each gland begins at a slightly constricted surface orifice, where its cells are of much the same type as those of the surface, but deeper down they become elongated and columnar. Descending to variable depths, the terminations of the longest sometimes dip into the intermuscular spaces, sometimes turn and run at right angles with their beginnings, and parallel with the myometrium. Although some, especially the French, histologists look upon these as pseudo-glands—glanduliform depressions—they seem to secrete an alkaline mucus.

The stroma also contains occasional small lymph follicles that must not be mistaken for inflammatory collections or miliary tubercles.

III. *Physiologic Variations in the Endometrium.*—These are of the greatest importance, and the source of most of the errors in diagnosis to which reference was made above.

With the approach of each menstrual period, the endometrium is stimulated to a kind of proliferative evolution that reaches its maximum about the time that the flow begins, and then following the saturation by blood, terminates in an involution during which it returns to the "resting state." As these changes occur simultaneously with what goes on in the ovary at the same time, it seems proper to infer that one may be the cause of the other. A sensitized and hypertrophied endometrium can be imagined greatly to facilitate the embedding of the fertilized ovum, and as it progresses further in cases in which impregnation is effected, and recedes when it fails, it seems reasonable to conclude that the evolution of the endometrium takes place with that end in view.

The evolution of the endometrium according to this conception results in the formation of a considerable sized endocrine gland, for it swells to some six or more times its usual thickness, becomes distinctly visible to the naked eye, and persists and increases even though the product of conception be detained in the Fallopian tube, and never admitted to the uterus at all.

The normal endometrium of the reproductive period of life, therefore, has a variable appearance, corresponding with its cyclical changes. It is almost constantly changing, but its period of least variability, and most constant appearance, is that known as:

1. *The Intermenstrual Period.* This varies from about the 14th to the 21st days after menstruation. During it the endometrium of the corpus uteri is from 0.5 to 1.0 mm. in thickness. Its surface is covered with a single layer of cuboidal or cylindrical cells, ciliated except for occasional areas. At intervals of every 0.1–0.2 mm. the epithelium dips down into the subjacent stroma to form the glands, gradually changing its type as it descends, being more cuboidal at their mouths, more distinctly columnar below. The cells of the glands are said to be ciliated, but if so, the cilia are very rarely seen, probably requiring special methods of preparation to define them.

The glands are said by Frank to be 40–50 microns in diameter, and 1–2 mm. long. They descend perpendicularly until near the muscular wall of the organ, when they commonly bend and course a short distance horizontally, or parallel

with the myometrium. They may be simple or have a few bifurcations and their walls are straight in the sense that they are usually without any papilla-like projections. The cells rest upon a well-defined basement membrane, have clear cytoplasm, and contain well-staining vesicular nuclei that are nearest
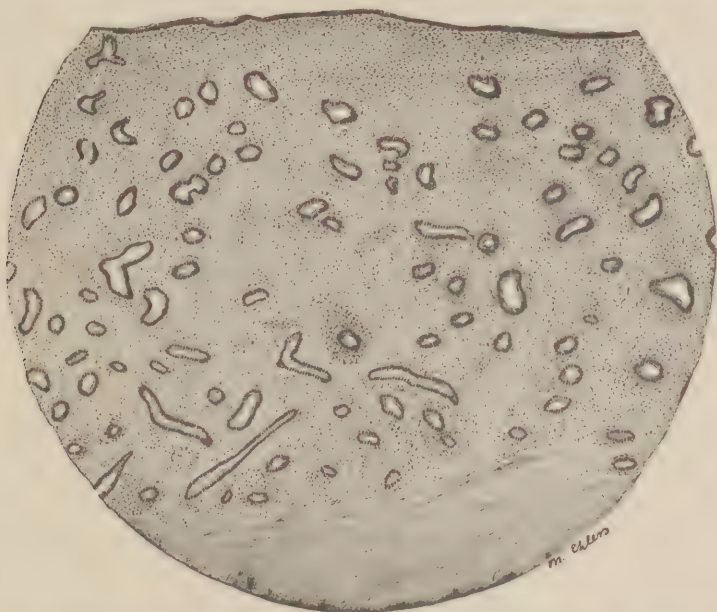
FIG. 349.—Resting endometrium of a virgin. Most of the glands are transversely cut. The illustration shows the relative proportion of glandular and interglandular tissue, as well as the breadth of the glands. It does not show their length. (*Aschoff*.)

the center in the more cuboidal cells, and nearer the basement membranes in the more columnar cells. The lumina of the glands sometimes contain a trace of alkaline mucus.

2. *The Pre-menstrual Period.* From four to six days before the beginning of the menstrual flow the endometrium begins to show enlargement first of individual glands, then gradually of all of the glands, which increase in diameter and in length as shown by a remarkable degree of tortuosity. The increase in diameter brings them closer together, and makes them appear more numerous, and they soon become filled with secretion. This appearance is commonly described as "glandular hyperplasia," and has been called "*hypertrophic endometritis*" under the misapprehension that it is an evidence of morbid change.

Upon more careful examination it will be found that all parts of the thickness of the membrane do not show uniform involvement, and that it is possible to divide it into an outer *compact* layer, a middle or *spongy* layer, and an inner *unchanged* layer. The compact layer is characterized by considerable swelling of the stroma, without associated swelling of the glandular tubules.

The general appearance of the *stroma* is edematous, but that is not all. Its cells, both round and spindle, are found to have developed visible cytoplasm,

so that they are larger than before, have more distinct outlines, and are more widely separated from one another. These transformations are most distinct below the surface epithelium, and in the vicinity of the capillary blood-vessels that now begin to appear more numerous and larger. Why the glands do not enlarge in this layer is not known, but it may be that only the secretory cells are stimulated, and that they are below, the cells of the compact layer being only a continuation of the surface epithelium. The inner layer appears as in the inter-menstrual period, and shows little if any change.
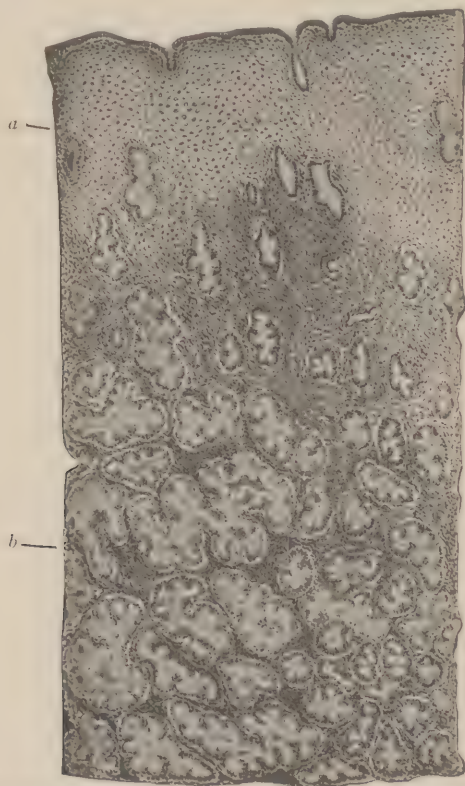
FIG. 350.—Premenstrual swelling of the endometrium. *a*, Compacta; *b*, spongiosa, with papillary elevations in the dilated glands. This normal condition is frequently mis-called *hyperplastic endometritis*. (*Aschoff*.)

The enlarged and distinct stroma cells are commonly spoken of as *decidual cells*, and their presence was at one time thought to be pathognomic of pregnancy. With it, however, they have no more definite connection than the other modifications described. However, if pregnancy occur, whether in the uterus or elsewhere, these cells increase enormously both in size and number until the endometrium, now the decidua, comes to bear a resemblance to an epithelial endocrine organ—which, indeed it may be.

3. *The Menstrual Period.* This is characterized by added edema of the tissue, turgescence of its capillaries, and the escape of blood corpuscles with which the entire structure becomes saturated. It is hemorrhage by diapedesis,

but whether the blood corpuscles penetrate the vessel walls without minute ruptures, or escape through such is not known. The escaped corpuscles are expressed through the surface epithelium, sometimes are squeezed into the glands, and eventually thus brought into the cavity of the uterus from which they escaped mixed in the secretion of the glands, to form the menstrual discharge. Some inhibiting effect is produced by the tissues or their secretions, so that the menstrual blood does not coagulate.

With the escape of the blood and edematous fluid, together with the contents of the glands, the swelling and pressure are relieved, and the next stage begins.

4. *The Post-menstrual Period.* During this short period, the membrane returns to normal—i.e., to its resting state—and the inter-menstrual period once more develops. Some think that by the close of the menstrual flow the endometrium is already recovered from its evolution, and needs no subsequent involution. Others see in this stage only the final cleaning up and quiescence. Blood corpuscles disappear from the tissue, secretion from the glands, the latter contract to their former dimensions, the swollen stroma retracts, and within a period of a few hours in some cases, a few days in others, the inter-menstrual period is reached.

It was formerly taught that with each recurring menstrual period the entire endometrium was destroyed and then regenerated; later it was supposed that the greater part of it thus suffered destruction and regeneration, but as the result of modern investigation it has come to be believed that the function of menstruation is not destructive to the endometrium, and that it suffers from no other disturbance than periodic excesses of hyperemia and hypersecretion without destruction and needing no regeneration.

To these pictures, any of which may be shown in endometrial scrapings must be added still more complicated as well as more unusual ones that may occur when the curettage is taken from cases of extra-uterine pregnancy or post-partum cases with retained secundines, and to understand them it will be necessary still further to pursue the variations of the endometrial tissue.

In pregnancy the conditions vary according to its duration. In the early months, the compact layer increases both in thickness and the size of its component cells until it becomes distinctly like an epithelial tissue, and this development of the decidual cells is not confined to the compact layer, but descends so deeply that most of the stroma of the well developed spongy layer is also made up of decidual cells though replete with large glands. The glands also take on a new appearance. In the endometrium of menstruation, the enlarged glands of the pre-menstrual period though distended and serpentine, and having occasional small papillary projections interrupting the smoothness of their walls, nearly always maintain a fairly regular layer of uniform cells. But with the occurrence of pregnancy, the enlargement of the cells becomes still greater, their form changed, and neighboring cells crowded out of the row to which they belong, appear as collections of clavate cell members attached to the basement membrane by slender connections, thus forming eminences that give the interior of the glands a decidedly papillary appearance—"*Gebhard's glands.*" At one time these were considered to be characteristic of pregnancy, but it is

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now known that they sometimes occur in pre-menstrual activity. However, if the decidua is excessively developed, and the Gebhard's glands plentiful, pregnancy may be suspected, and if such occur without evidences of syncytium or chorionic villi, ectopia of the ovum should be suspected.

As the weeks go by, and the ovum, embedded in the decidua vera becomes covered by the decidua reflexa, and the ovisac enlarges, additional changes
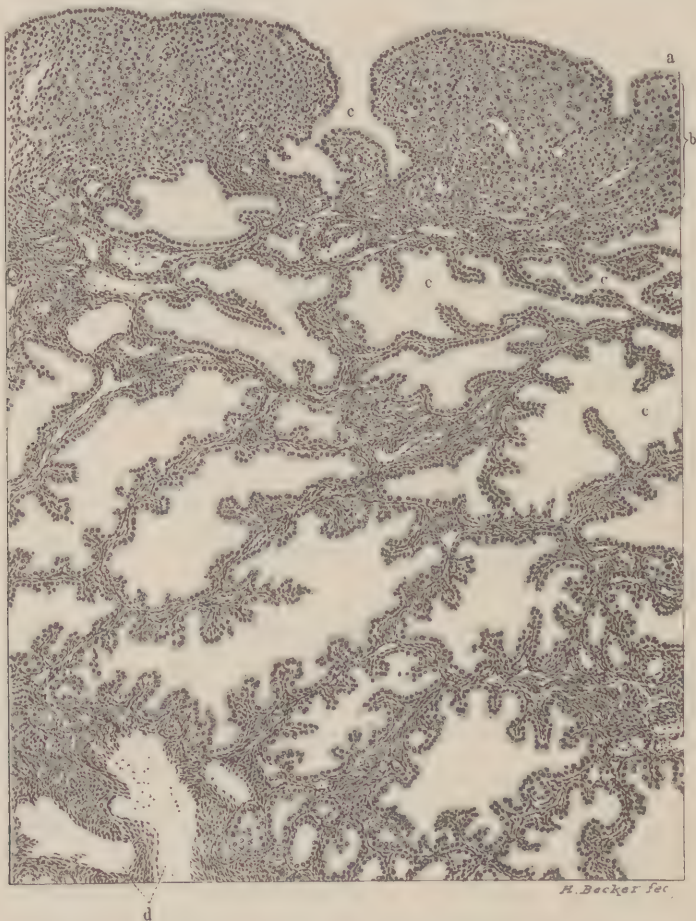
FIG. 351. —Decidua of pregnancy, showing the entire thickness of the membrane. *a*, The covering epithelium; *b*, the decidua compacta; *c*, spaces in the decidua spongiosa; *d*, veins at the margin of the muscular tissue below. (*Cullen*.)

occur. The surface epithelium separating the two layers of the decidua disappears, pressure effects atrophy of the remainder of the decidua vera which becomes flattened out and thinned, while the blood-vessels about the site of implantation, especially the veins become numerous and large.

As is well known, the nidation or implantation of the ovum results from activities on the part of its own tissues, the chief of which is a cell collection at one pole known as the syncytial knob or *trophoblast* which seems possessed

of the power of eroding the decidua so that the ovum sinks into it, to become later surrounded through the union of the surrounding suprajacent undisturbed membrane, which becomes the decidua reflexa—*decidua capsularis*. As the ovum becomes embedded, capillary blood vessels of the decidua are subjected to the solvent action of the syncytium, and blood escapes, surrounding the embryo with a hemorrhagic area supposed to provide its cells with their first
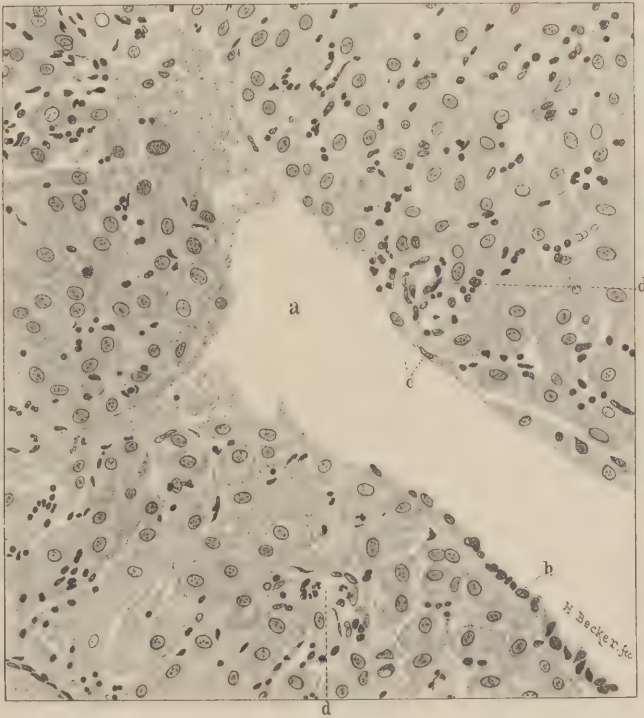
FIG. 352.—Normal decidua compacta. *a* is a section of a large vein containing some blood in its branches. Its walls consist only of endothelium, somewhat heaped up and distorted at *b*, swollen but still intact at *c*.). Delicate capillaries are indicated by *d*. (*Cullen.*)

supply of food. From the trophoblast, cell cords next seem to extend into this blood space, dividing it up into an irregular network, more or less branched, and composed of synctytial cell masses in the form of plasmodia. Such syncytial plasmodial ramifying and communicating extensions occur on all sides of the ovum, and become penetrated by extensions of the chorionic mesoderm, and develop into the chorionic villi, which give the outer surface of the ovisac its shaggy appearance. As they further develop each villus comes to consist of a central core of mesoderm, composed of a delicate mucous tissue containing blood-vessels, covered by a double layer of cells derived from the embryo, the inner of which, regularly cuboidal in shape, and pale in color in stained sections, comprises the "*cells of Langhans;*" the outer, forming an indefinite plasmodium, thicker in some places than in others, as the age of the embryo increases, becomes divided into more or less separated masses, some of which resemble giant

cells, and all of which appear dark and basiphilic in stained sections, the remains of the trophoblast, the *syncytium*. As the age of the ovum increases the villi become more and more distinctly provided with blood-vessels.

At first the villi of the chorion entirely surround the ovum, but as it develops, they become separated into groups—the cotyledons—through the growth of trabeculae from the walls of the uterus into the intervillous space. This affords those villi on the side of the ovisac adjacent to the deeper tissues of the uterus
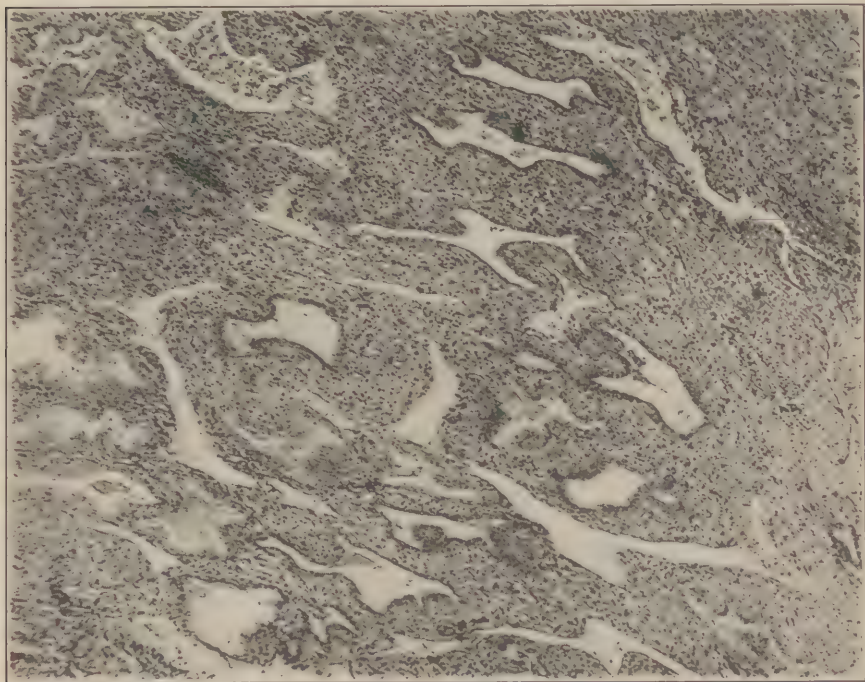
FIG. 353.—Microscopic section of the decidua of pregnancy showing the spongiosa only.

an opportunity to outgrow their fellows, and to implant themselves deeply into the uterine tissues and vessels. It is at the point of implantation of these villi that the placenta subsequently develops, and elsewhere the chorionic villi disappear. The deeply implanted villi, may lose the layer of cells of Langhans, and become surrounded solely by syncytium.

When the uterus is curetted in early pregnancy, as in cases of abortion, the tissues coming for examination have an appearance strikingly different from those from a non-pregnant organ. The greater part of the tissue will be found to consist of decidua from the compact layer, with occasional areas in which the large glands of Gebhard appear, but what is of supreme importance is the presence of more or less well formed chorionic villi surrounded by their layers of cells of Langhans and syncytium.

In cases of later pregnancy and where there are retained secundines following parturition, far greater quantities of material are usually obtained, consisting
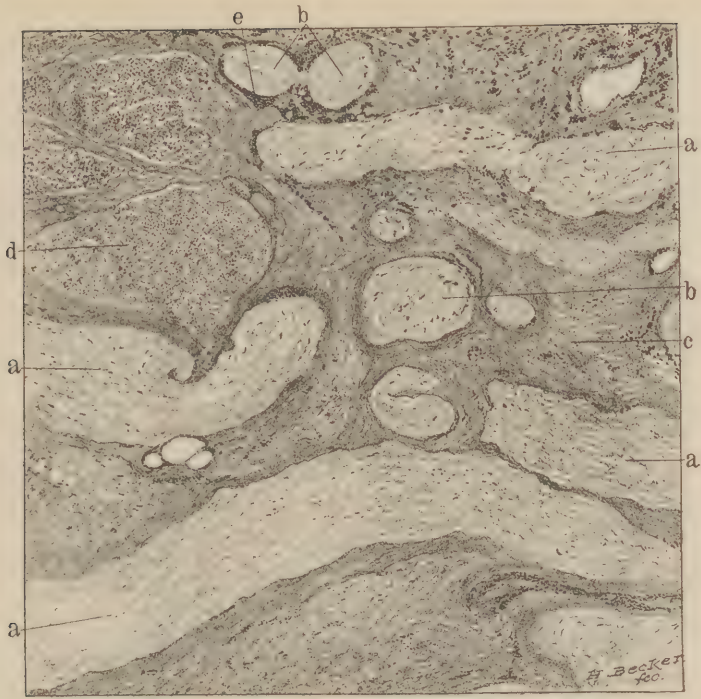
FIG. 354.—Placental villi retained some weeks in the uterine cavity. *a*, Longitudinal; *b*. transverse section: *c*, canalized fibrin between the villi; *d*, venous sinus. (*Cullen.*)
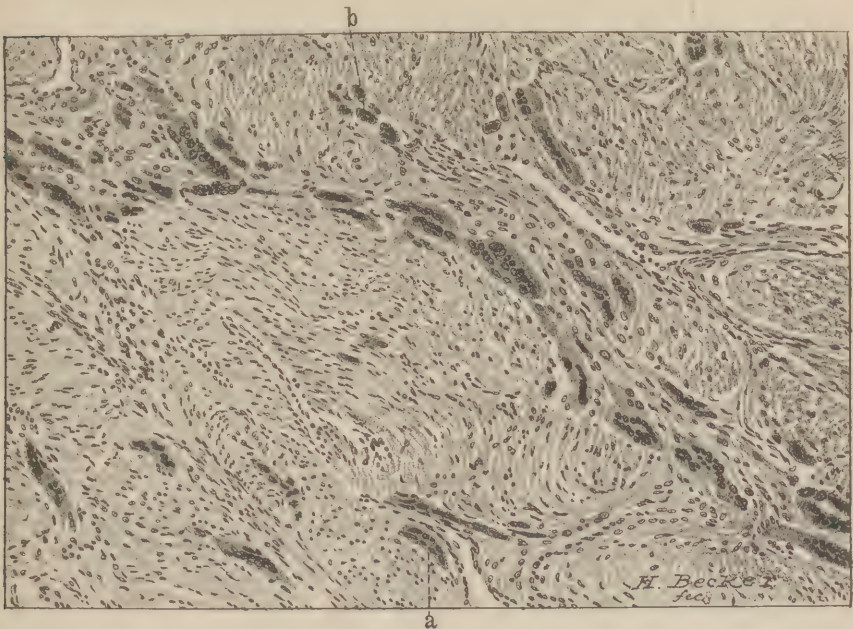
FIG. 355.—Decidual giant cells, *a* and *b*, in the underlying uterine muscle of a pregnant uterus at full term. (*Cullen.*)

chiefly of fragments of the placenta.   Much of this tissue may be highly necrotic and unrecognizable, but usually well preserved fragments can be discovered.

During the implantation of the ovum, and following it, during the development of the placenta, the columns of cells constituting the foundation of the chorionic villi, and composed of syncytium, find their way deeply into the intermuscular spaces of the myometrium, where they seem capable of remaining throughout the pregnancy, and sometimes for years subsequently.

FIG. 356.—Chorionepithelioma of the uterus (½ natural size).   (*Johres.*)

The discovery of syncytial tissue in the myometrial fragments removed by the curet from the uterus of a woman with the history of continued post-partum bleeding, with the presence of an enlarged uterus containing a fleshy mass removed by the instrument, always raises the question whether the case may not be one of *syncytioma* or *deciduoma malignum*.   The question is always asked, and is sometimes answered with an assurance that would suggest a diagnosis easy to make.   As a matter of fact, it is most difficult, and we believe rarely possible.   There are no definite criteria by which the malignancy of the condition can be recognized.   Syncytioma malignum is a clinical, not a pathological condition.

Moreover, the pathological histology of the chorionic epithelioma, deciduoma malignum or syncytioma malignum is so variable that no two cases appear

precisely the same. This might be expected when the structures implicated are remembered. There is first the decidua, then the chorionic villi with their cells of Langhans, and the syncytium, then there are the syncytial cell columns or ribbons. These, confused in arrangement both quantitatively and qualitatively, mixed with considerable quantities of blood, and frequently in a state of advanced necrosis by which the whole picture is, masked, give very little precise
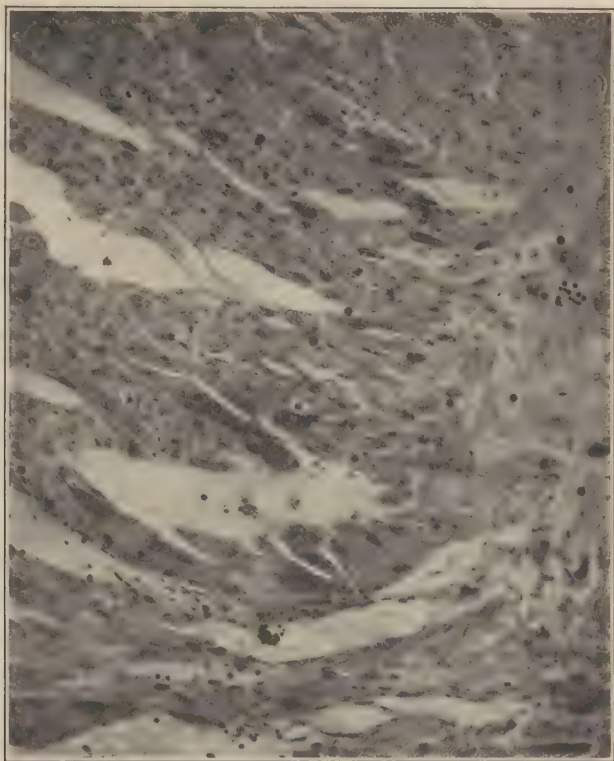
FIG. 357.—Chorion-epithelioma or syncytioma malignum. (*Photomicrograph by Prof. Allen J. Smith.*)

information. Not a few cases diagnosed as highly malignant tumors, have never been heard from after the uterine cavity has been emptied of its contents with the curet. A few cases thought to be benign have died with wide-spread metastases.

Endometrial curettage is also performed for the purpose of assisting the diagnosis of *cancer of the body of the uterus.*

In this disease the endometrium becomes thickened, its surface mammillated, and not infrequently covered with villous excrescences. The quantity of material removed for examination may, therefore, be considerable. In well marked cases the diagnosis can usually be made without difficulty, but there are exceptions, as, for example, where very little tissue is found among the blood clots, where the tissue is highly necrotic, where an endometrial polyp has been

removed, and where the endometrium is hyperplastic and bears a close resemblance to pre-menstrual activity.

Carcinoma of the body of the uterus may be of the squamocellular, rotundocellular or cylindrocellular varieties. The first is extremely rare and so characteristic that it ordinarily presents no difficulty of diagnosis. The second, carcinoma rotundocellulare, seeming to develop from the glands after neoplasmic metaplasia, is not frequent, and being composed of cells arranged in solid
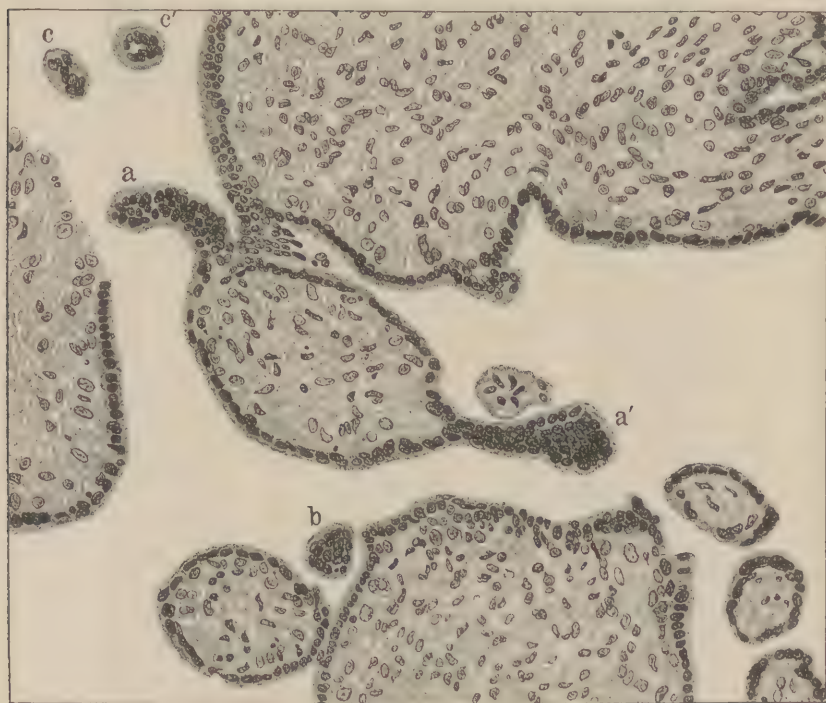
FIG. 358. — Normal placenta at about the twelfth week, showing the villi, and the syncytial buds *a* and *a′*, cross sections of which produce the so-called syncytial giant cells *b*, *c* and *c′* (*Cullen.*)

acini, presents the usual picture of cancer, and should also be distinctive. But the third variety, the carcinoma cylindrocellulare, may puzzle the most experienced at times. It occurs in either of two forms; first the variety of tumor. sometimes called *destructive adenoma* in which with an enormous increase in the number of glandular elements, which invade and destroy the adjacent tissues and effect metastasis, the relation of the cells to the basement membrane is preserved for a long time, and second, the typical adeno-carcinoma, in which the histological structure differs widely from the normal type from the very beginning, though a more or less definite glandular type of structure is preserved.

To make the diagnosis it is well to begin by excluding certain conditions that that may give false impressions.

1. *Uterine Endometrial Polypi.*—These occur singly or in small numbers, and may be removed entire. A frequent variety consists of an elongate finger-like process, perhaps a centimetre or more in length, smooth and rounded, dark red in color, that shows, under the microscope, a structure that corresponds fairly well with that of the endometrium, though somewhat exaggerated as to
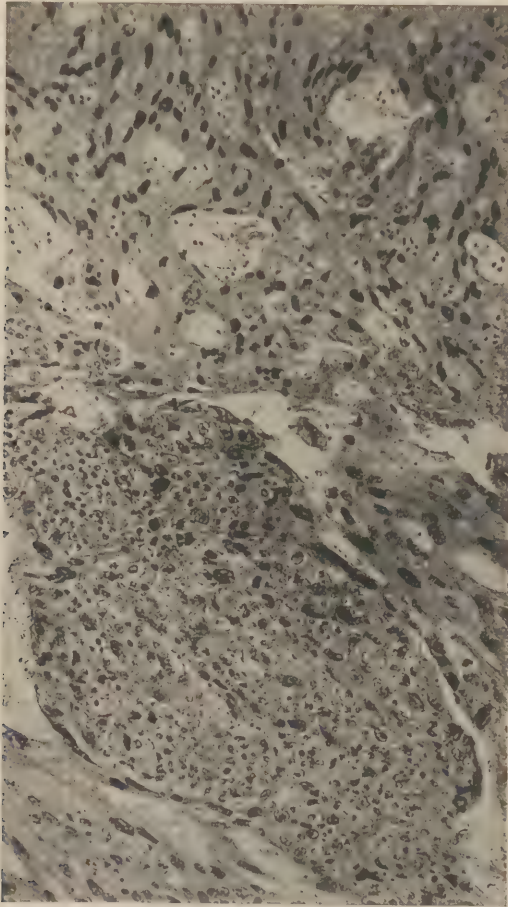
FIG. 359.—Choriocarcinoma. Above, masses of syncytial cells resembling squamous epithelium. Below, group of Langhans' cells. (*Ewing.*)

details. Nearly all of these are benign. There is also a second, more rare variety of polyp, corresponding with the papilloma of the digestive and respiratory mucous membranes, and consisting of a tuft of branched villi arising from a narrow pedicle. These frequently show more or less irregularity of structure yet fail to give the usually accepted indications of malignancy. As upon the other mucous membranes, though what is seen in them gives the impression of benignancy, what may have been beneath them in the mucosa from which they arise is the important matter. In most cases such formations indicate carcinoma of the deeper structures. The histological structure of other bits of tissue shou.

always be looked for to evidence this, but in their absence, malignant disease may be assumed to exist.

2. *Normal endometrium in the state of activity incidental to the pre-menstrual period*, or resulting from the continued stimulation associated with the presence of uterine fibroids or other chronic disturbances. Here the richness in glands, their close approximation, the irregularities in their apparent structure resulting from branching and especially the presence in their tubules of small papillary projections, and the active secretion must be taken into account.

3. *Inflammatory disease of the endometrium with leukocytic infiltration* not infrequently results in the dissociation of the cell linings of the glandular tubule with irregularities sometimes easily mistaken for malignant disease.

4. *Artefacts effected by the mechanical action of the curet* not infrequently result in pictures resembling malignant disease, and must be carefully excluded.

But the diagnosis of carcinoma does not only depend upon the discovered irregularities of histological detail; it also depends upon cytological variations and details. The cells of carcinoma are actively vegetative. They lack their normal clear and colorless cytoplasmic appearance, and, though not always granular, assume a slightly basophilic or polychromatophilic quality. They also appear crowded, and in many areas are found to occur in several layers, or to aggregate in mass formation in the lumina of the carcinomatous acini. The nuclei are rich in chromatin, and instead of being centrally situated, or regularly disposed along the basement membrane, occupy either pole of the cell indifferently. Moreover, with the abnormal richness in glands there is little evidence of increased secretory activity: the lumina of the glands are empty.

The surgical pathologist is also frequently consulted with reference to the benignancy or malignancy of lesions of the cervix uteri. It is therefore necessary to be familiar with the histological peculiarities of the mucosa of the isthmus and the cervix, as well as with those of its body.

The region from the internal to the external os uteri constitutes its isthmus, and is lined with a mucous membrane that may be regarded as transitional between that of the body and that of the cervix. It is relatively thinner than the endometrium proper, and although it possesses the same layers, each is thinner. The surface epithelial cells generally tend to become more definitely cylindrical, and the glands to be shorter, though both short glands like those of the cervix and long glands like those of the endometrium proper may be present. The stroma is thinner and less cellular, or nuclear as the case may be. Just within the external os the highest columnar cells occur, and at a variable point just outside of the external os they suddenly join the squamous epithelium of the portio vaginalis cervicis.

The exact point of juncture differs in different individuals. In some the squamous epithelium seems to enter the os for a short distance; in others the columnar epithelium spreads externally upon the portio vaginalis for a considerable distance. These are natural conditions, but may be simulated or exaggerated as the result of injuries incidental to parturition.

Thus, where the os is dilated, and especially where there are multiple lacerations, the endometrial mucosa may appear externally, giving the tissue a granu-

lar red appearance—so-called granular erosion of the cervix. On the other hand, under the same conditions, the squamous epithelium may grow into the cervical canal for a short distance. Whether the result of individual peculiarity or the result of laceration, the appearance of the red granular isthmian mucosa upon the external surface is called *granular erosion, eversion* or *ectropion*.

Fig. 360.—Meeting point of normal and carcinomatous epithelium in squamous cell carcinoma of the cervix uteri. *a*, Normal epithelium of the vaginal portion of the cervix; *b*, two cross sections of papillae; *c*, the point at which the normal cells merge with those of the tumor, and when they are closely packed together. The nuclei stain deeply, and at *d* and *g* not only contain an increased amount of chromatin, but are also enlarged. *e* is an elongated papilla; *f* shows necrotic tissue on the surface. The stroma *h*, underlying the normal mucosa shows no alteration, but that beneath the carcinomatous portion shows considerable small round-cell infiltration as indicated at *i*. (*Cullen*.)

As the termination of the cylindrical cell covered tissue is reached and the squamous cell covered portion of the cervix comes under examination, a change is observed in the glands. They become shorter, and no longer form simple tubules, but are branched. The squamous epithelium dips into their mouths for a very short distance, then immediately gives place to a beautiful columnar epithelium resting upon a distinct basement membrane, the cells invariably in single row, with the nuclei low down. The cytoplasm of the cells is clear, devoid of basophilic tendency. But when, either at the menstrual period, or at any other time, there is exaggerated secretory activity, the whole picture may change. The glands then seem to increase both in size and in number, the epithelial lining to be thrown into folds, and the cells to become granular from

the presence of mucins, while the interiors of the acini become distended by a mucinous secretion so thick that it frequently has difficulty in escaping and individual glands may become distended to a size as large as peas or small cherries, forming the so-called *follicles* of *ovules of Naboth*. The secretion seems to take place at the expense of the cells which transform into mucus, and fray out, some detaching before their transformation is complete, so that it is not unusual to find numerous cells, some with nuclei, in the secretion. Goblet cells usually do not occur except in the cells of the ducts.

The glands are embedded in a corium that is the homologue of that of the endometrium, but is thinner, and much less nuclear or cellular.

When the glands are quiescent their walls are smooth, and the acini though elongate, are regularly rounded: when they are actively secreting, they appear complex, and their walls are beset with small papilla not unlike those observed in the Gebhard's glands of the endometrium.

The squamous epithelial layer covering the portio vaginalis uteri is smooth upon its external surface, but being a stratified transitional tissue, is supported upon a corium with a more or less well developed papillary layer, into which occasional epithelial pegs dip down.

Two chief forms of carcinoma occur at the cervix—the squamous cell carcinoma of the surface covering, and the glandular carcinoma, or adeno-carcinoma.

As more cases are sent for examination on account of suspicion than for actual confirmation, the pathologist should be prepared to recognize as nearly as possible the first signs of malignant diseases. He must, therefore, begin by excluding such conditions as may be benign in nature, but apt to lead him into error.

1. *Tangential, instead of vertical cutting of the section*, increases the apparent thickness of the epidermal covering, and introduces many sections of the epithelial pegs, misleading the novice into believing that he is dealing with epithelial proliferation.

2. *Nature's attempts to repair lacerations of the cervix* result in the descent of the epithelial tissue into the irregularities of the tear, sometimes in a very misleading manner.

3. *Inflammatory disease of the cervical tissue following lacerations*, fills its stroma with leucocytes, destroys the basement membrane of the glands, and permits their cells to undergo more or less dislocation and separation sometimes difficult to differentiate from malignant disease.

4. *Traumatic dislocation of tissue elements* when the material to be examined was removed with the curet.

The most frequent tumor of the cervix is the squamous cell carcinoma. It arises where squamous epithelium occurs, i.e., upon the portio vaginalis. It is possible, however, for it to first make its appearance in the cervical canal.

It is characterized by what appears to be simultaneous downward growth of epithelial pegs, and upward papillary excrescence from the squamous epithelium. The result is a superficial mass that is soft and friable, and a deeper invasion that is hard. There may be benign papillomas of the cervix that bear microscopic resemblance to these excrescences of carcinoma, but they must be very

rare, and it is usually wise to regard such as indicative of malignant disease. The typical excrescences of carcinoma are finger-like and branched. Each consists of a central core of fibro-vascular tissue, and an outer many layered covering of transitional epithelial cells. Caught between the processes are quantities of muco-pus, blood and degenerated cells, sometimes with epithelial pearls. The deeper infiltrating portions may be of the basal cell type of structure, or without definite prickle cells show marked keratosis with small or large

FIG. 361.—Squamous cell carcinoma of the cervix uteri. A "cauliflower" mass, springing from the anterior cervical lip ($\frac{1}{2}$ natural size). The uterus and appendages are seen from behind. Attached to the anterior lip by a broad base is a fungous growth composed of small, rounded, semi-translucent masses. It resembles somewhat a bunch of grapes. The posterior lip is entirely free from the growth. The uterine arteries have been tied at a distance from the cervix and are seen sending off their various branches to it. The uterus is of the usual size; the tubes and ovaries are normal. The small cyst projecting from the neighborhood of the fimbriated extremity of the right tube is the hydatid of Morgagni. (*Cullen after J. G. Clark.*)

epithelial pearls sometimes in small, sometimes in great numbers. The downward extension may be effected by enlargement of the epithelial pegs which branch and ramify, or it may be associated with invasion of the mouths of the glands into which it grows and which it eventually partly or completely fills. The growing cells crowd one another, and soon necrosis and ulceration follow, and there is a highly characteristic and very offensive discharge from the vagina. The disease extends downward and forward to the vagina, and backward to the rectum and bladder, causing difficult defecation and micturition, and sometimes effecting communications—fistulas—between the affected viscera. Sooner or later the pelvic and retro-peritoneal lymph-nodes are affected, and in some cases secondaries occur in the liver, more rarely in the lungs. The patient slowly becomes exhausted from loss of blood from the ulcerated and necrotic lesions, infected through the ulcerations, intoxicated through the absorption of the necrotic material as well as through the disturbances of the rectum and kidneys, falls into profound cachexia, usually to die from some intercurrent affection such as pneumonia or nephritis rather than directly from the cancer.

The more rare cases in which the tumor springs from the external os or arises within the cervical canal manifest no essential difference in the pathological or clinical picture once the disease becomes established. The diagnosis is, however, more apt to be made from curettage than from excised fragments of the cervical tissue.

As adeno-carcinoma usually occurs where epithelial glands are normally found, and as we have seen that they occur upon the cervix, even where its
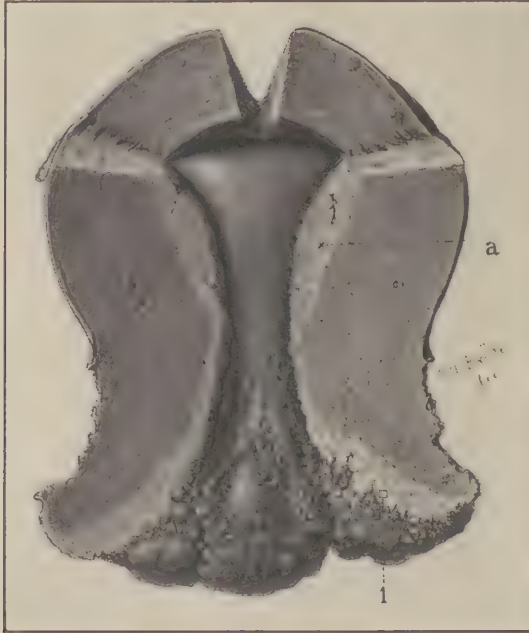
FIG. 302.—Adeno-carcinoma of the cervix uteri, with extension to the polyp *a*, and to both uterine horns. (*Cullen.*)

surface is covered with squamous epithelium, it is not surprising that they may occur either from the tissues of the cervical canal, where they are perhaps more common, or from the portio-vaginalis where they are more rare.

If the tumor spring from the former, it may attain to considerable size before it escapes from the cervical canal and become visible as a fungus mass; but if it arise from the latter, it immediately becomes visible as a fungous or cauliflower mass, soft in consistency, red in color, and friable to the exploring finger. In the first instance the diagnosis may be made from scrapings removed with the curet, in the latter from actually excised fragments of the mass itself.

The same diagnostic features apply in the case of adeno-carcinoma of the cervix as were given for the recognition of adeno-carcinoma of the body of the uterus. But in order that the earliest changes may be recognized, it may be well to quote from Cullen's "Cancer of the Uterus" as follows:

"The epithelial cells begin to multiply and form teat-like or club-shaped growths, project-ing into the lumen. These excrescences gradually unite with one another to form small glands.

Fig. 363.—Microscopic section of the adeno-carcinoma of the cervix shown in the preceding illustration. *a* and *b*, Main glandular trunk; *a'* and *b'*, branches; *c*, transverse sections of terminal outgrowths; *d*, epithelium in multiple layers; *e*, in single layer; *f* and *g*, stroma. (*Cullen.*)
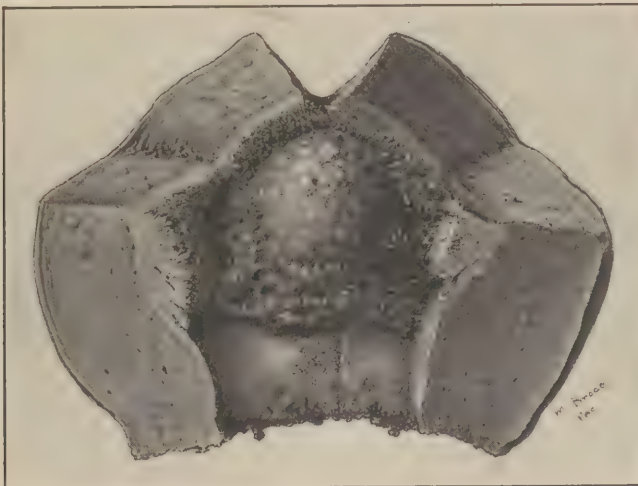
Fig. 364.—Adeno-carcinoma of the body of the uterus. (*Cullen.*)

Thus, within one-third, two-thirds of a gland, or an entire gland, from the multiplication of the epithelial cells may be formed twenty or thirty small glands. Between these there is little or no stroma. The epithelial cells forming these new glands have oval-vesicular nuclei that do not stain very intensely."

As was the case with the squamous cell carcinoma, the tumor soon forms a cauliflower mass "composed of branching papillae, which have an abundant stroma consisting of spindle shaped cells, the outer surface being covered by one
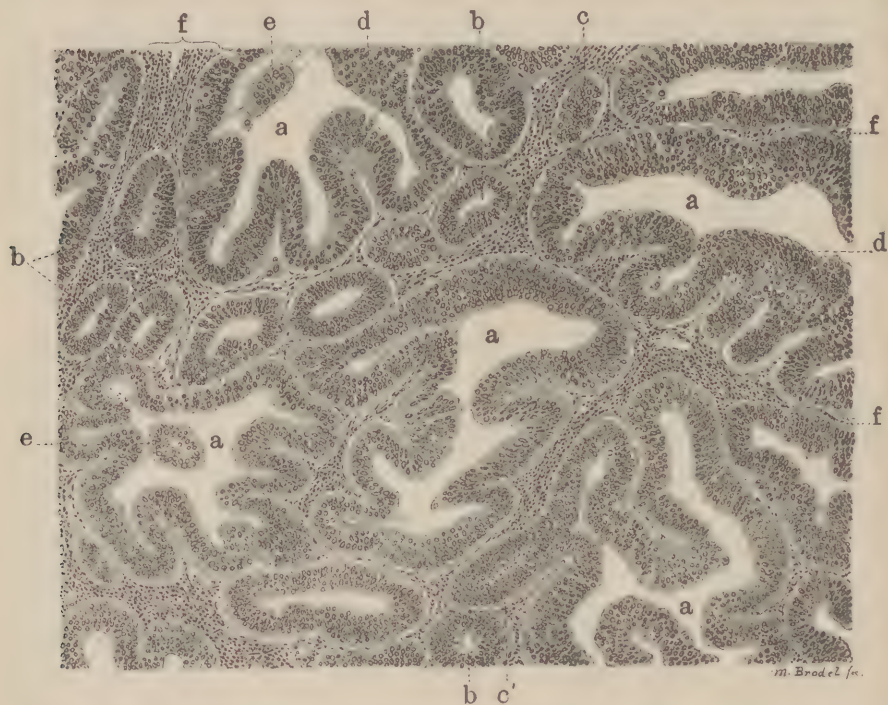
FIG. 365.—Microscopic section of the adeno-carcinoma of the uterus shown in the preceding illustration. *a*, Markedly convoluted glands; *b*, cross section of terminal glands; *c*, tangential section of terminal gland; *d*, epithelium in multiple layers; *e*, cross section of the top and of one of the folds; *f*, stroma. (*Cullen*.)

or several layers of cells continuous with those lining the glands in the depth." These papillae have a much more abundant stroma and a less abundant blood supply than those of a squamous cell sarcoma.

"The epithelium lining the glands and covering the papillary processes is multiform. It may consist of a single layer of cylindrical cells, having oval vesicular nuclei; or, when several layers are present, the cells become more polygonal. The cells as might be expected, contain nuclear figures in various stages. Not a few have two or three nuclei. In the degenerating cells karrhyorhexis is not infrequently noted. There may be such diversity in the forms of the cells that in some portions of the gland it is hardly possible to find two cells alike. At one point the gland is lined by cells approximately cylindrical, but the individual nuclei are of unequal size; in the adjoining cells the nuclei are relatively twice as large, while a little further on, the cells are represented by extensive plaques of protoplasm, each containing a large laminated mass of chromatin. Some of the epithelial cells on the opposite side of the gland are spindle-shaped. In general it may be said that the epithelial cells in adeno-carcinoma of the

cervix differ greatly from those of the normal cervical epithelium, and cannot, morphologically, be recognized as derivatives from it. The cells and nuclei may be of any shape or form; sometimes the nuclei stain faintly, at other times most intensely. Along the advancing margin of the growth the nuclei almost invariably stain very deeply."

"The stroma of the growth is composed of the cervical tissue, which is usually infiltrated with small round cells. This infiltration may be localized or general, but is most marked along the advancing margin of the growth."

In far more rare cases the curettage from the uterus, whether from the body of the isthmus, or even from the cervix shows sarcoma instead of carcinoma
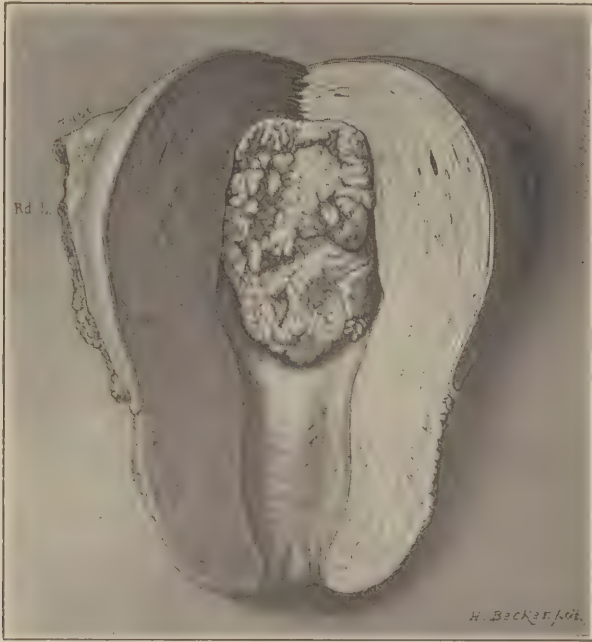
Fig. 366.—Round-cell sarcoma of the body of the uterus. (*Cullen.*)

structure. This is sometimes frankly composed of round cells, less frequently of spindle cells, and under these circumstances occasions no difficulty in making the diagnosis. But unfortunately not a few cases are non-de-script, and positive differentiation from carcinoma is impossible. This difficulty, and the unreasonableness of insisting that such a tumor must be either sarcoma or carcinoma is considered in the section dealing with tumors.

When the sarcoma is large enough to project from the cervix, or after operation or autopsy is displayed for examination by opening the organ, it is found either to be a smooth pale colored tumor of homogeneous structure, or one whose surface is covered with bosselations or more rarely finger-like projections. When composed of round cells it may be soft, when of spindle cells, firm. There is lack of the differentiation into cells and partitions that characterizes the structure of carcinoma, but in not infrequent cases this, like other criteria

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may fail, and the observer be left in doubt of the true nature of the lesion. Occasional tumors have been called endothelioma, but of the validity of this diagnosis doubt may be expressed. In most of the doubtful cases it is perhaps best to regard the tumors as carcinomas. The matter is, however, of no practical importance, as both tumors are malignant, and the treatment the same.

A rare variety of uterine sarcoma of adults, perhaps having the same origin as the similar sarcoma botryoides vaginae, on account of its divided grape-like appearance, is known as Spiegelberg's "grape-like sarcoma." It is highly malignant.

Tuberculosis of the endometrium, and of the cervix is occasionally discovered through the examination of curettage and excised fragments. To the eye and examining finger it may appear so similar to carcinoma that the discovery of tuberculosis comes as a matter of surprise. There is, however, no difficulty about the microscopic diagnosis. The lesions are characteristic.

In the cervix it effects deep necrotic change with ulceration resembling squamous cell carcinoma. In the endometrium it descends to the myometrium, gradually effecting caseation of all the tissue down to the serous coat, and even this may become involved

Fig. 367.—Grape sarcoma, or sarcoma botryoides. The vagina is seen crowded with grape-like masses of the growth. (*Graves, copied from a drawing in Küstner's Handbuch.*)

so that the uterus may perforate. Some years ago Dr. W. W. Babcock, showed me a uterus from the Kensington Hospital for Women, service of Dr. Charles P. Noble, that had been removed from a little girl. It was of about the normal size and external appearance, but the entire interior had become transformed into a creamy pulp from endometrial and myometrial tuberculosis.

The disease seems sometimes to occur primarily—i.e., in those not seeming to be affected with tuberculosis elsewhere, or it may be secondary to pulmonary of other forms of tuberculosis. Not infrequently the Fallopian tubes are simultaneously affected.

Occasionally the surgical pathologist is embarrassed by the receipt of fragments removed from the uterus by the curet, that show no recognizable structure when sectioned and microscopically examined. Such material usually consists

of irregular pieces of tissue of considerable size, associated with hemorrhage, and superficial inflammation.

There seem to be two sources for such material, retained placenta, and necrotic sub-mucous fibroids. The former may sometimes eventually be determined by noting the presence of numerous larger and smaller rounded areas in the section, representing sections of the placental villi, the latter by noting that the tissue is resolvable into curling parallel formations that are the vestiges of the bundles of muscle cells.

DISEASES OF THE FALLOPIAN TUBES

From the broadest part of the uterus near the fundus, there extends laterally on each side, a structure representing the upper unfused portion of a Müller's tube, and known as the Fallopian tube. It is about 10 to 12 cm. in length, narrowest near the uterus, and broadest at its distal termination where it forms an infundibulum. The diameter varies from 0.3 to 1.5 cm. at different parts. It is covered externally by peritoneum derived from the broad ligament of the uterus, at the upper edge of which it is attached. Its structure consists of an outer longitudinal and an inner circular muscular coat derived from the uterine muscle, or at least connected with it, and its lumen which is continuous with the uterine cavity, is lined with a mucous membrane covered with ciliated columnar epithelium. As the diameter of the tube increases from the uterus outward, the mucosa becomes more and more rugose, being thrown into primary and secondary folds of great complexity as the ampulla is reached.

The Fallopian tube, which is the oviduct, or genital duct of the female, connects the uterus with the ovary, but although in a sense the duct of the genital gland, it does not connect directly with it except through a delicate elongation of one of the fimbriae surrounding the trumpet shaped external ostium, the *fimbria ovaricum.* The tube therefore terminates in an open infundibuliform extremity that forms a passage-way from the abdominal cavity through the uterus and vagina to the exterior.

A ripe ovum escaping from its ruptured Graffian follicle finds its way into the infundibulum of the tube partly through the erection of the fimbriae which brings the ostium in closer juxtaposition to the ovary, partly through the grooved surface of the fimbria ovaricum, partly through the aid of the descending current of fluid that at that time descends the tube, and partly through the aid of the cilia of the epithelial cells of the lining membrane.

The most frequent diseased conditions of the tube result from infection. Micro-organisms of disease may reach the structure, first, and most frequently from below—ascending infection—second, from its blood and lymph supply, and lastly from above, from the peritoneal cavity.

Acute salpingitis, or inflammation of the Fallopian tube, is only occasionally seen at either operation or autopsy: the chronic form is very frequent.

In the former the tube is swollen, reddened, elongated, tortuous, with an edematous thickened wall, and a circle of erect fimbriæ surrounding the infundibular end. From the interior, serous, bloody or purulent fluid may be expressed.

Longitudinal sections shows the lumina diminished through swelling of the mucosa which is red and edematous.

The latter, or chronic inflammation, is in all probability only a continuation of the same process associated with such changes as are incidental to it or occur in the attempts at repair.

Thus, at the fimbriate extremity the infundibulum is commonly lost, the fimbriae turn in, and the tube is found to terminate in a large rounded blunt extremity, that is usually adherent to the ovary and adjacent structures.

Concerning the closure of the mouth of the tube, Frank says:

"The simplest mechanism results when the ostium is blocked by peritoneal veils of adhesions, or adherence of the ovary or intestine to the opening. Retraction of the fibriae of the tube to within the inside of a hydrosalpinx or tubo-ovarian cyst has been explained by the fact that the fimbriae are the direct continuation of the intra-tubal folds. Inflammation through swelling and edema, causes functional occlusion at the right peritoneal ring situated at the base of the fimbriae. Distension of the temporarily occluded tube retracts the fimbriae into the tubal lumen, or the peritoneal surfaces of the ring thicken, the fimbriae are gradually squeezed inward and the narrowing ring allows of sero-serous adhesions producing permanent obliteration of the opening."

The exact appearance of the tube in so-called chronic salpingitis depends upon the duration of the process, and is therefore not easy to describe except in a general way.

The tube is usually elongated, tortuous, large in diameter, clavate, with little increase of diameter at the uterine ostium, but great increase at the other end which terminates in an immense rounded caecal pouch, which usually has many adhesions connecting it with adjacent structures. The wall may be either thick or thin. In the former case, usually representing an earlier stage of the disease, it may be hyperemic, edmatous, and infiltrated by leucocytes which cluster here and there in masses forming the beginnings of small abscesses. The interior of the sac is filled with puriform material that varies according to its age from frank pus to unrecognizable amorphus, granular and somewhat cheesy matter resulting from the disintegration of the pus cells. If the contents be removed and the surface of the mucosa examined, it will be found that the rougae have become immensely swollen from infiltration with the pus cells or that with the escape of those cells into the lumen have become flattened, adherent to one another, and largely destroyed. If the purulent exudation be large and remains, the result is the formation of a "pus tube," virtually an abscess surrounded by the walls of the Fallopian tube. Such may rupture, and discharge their contents into the abdominal cavity with results serious or otherwise according to the presence or absence of micro-organisms from the pus. Fortunately it is usually sterile. If rupture and evacuation does not occur, as in ordinary cases, the pus cells disintegrate, the fluid is absorbed, the content becomes cheesy, and calcification sometimes begins at the same time that the granular amorphus matter is being removed. The mucosa becomes thinner and thinner by atrophy and only occasional remnants of it may remain. At varying times regeneration of the epithelium is attempted, and is sometimes so considerable and so irregular as to resemble carcinoma.

Epithelial lined spaces resulting from the partial occlusion of rougae that have become adherent to one another not infrequently undergo cystic dilatation. Such epithelium is without cilia, is more often cuboidal than columnar in form and may become almost spherical, especially in those cases in which it proliferates.

The activity, extent and duration of the inflammation determine the sequence of events, and it is not possible to arrange them in any definite order. It is also unwise to divide the cases into groups described as catarrhal, interstitial etc.

The occasional abscesses of the wall sometimes result in the occurrence of nodular formations during the process of recovery—*salpingitis nodosa isthmica*, which is not a special variety of the disease.

Salpingitis is usually bilateral, and in most cases symmetrical, though the lesions may be more advanced or more destructive on one side than on the other. It usually results in sterility through the closure of the oviducts.

The great and common cause of the disease is gonorrhoea, though it is not always the gonococcus that is found in those cases that do not prove to be sterile. In the latter the infectious micro-organisms have died out; in others they have died out, but left associated and accompanying secondary invaders. But a few cases, following puerperal septic infection depend primarily upon strepto-cocci, staphylococci, pneumococci and other micro-organisms.

About 8% of the cases of salpingitis result from tuberculous infection.

TUBERCULOSIS OF THE FALLOPIAN TUBES

Tuberculosis of the female reproductive organs most commonly begins in the Fallopian tubes, without any more explanation than could be given for the primary occurrence of the disease in the epididymis in the male.

The disease is most frequent in those with early lesions in the lungs but as in the male, cases seem to occur independently of such, and appear primary.

In most cases there is so little difference between tuberculous and non-tuberculous salpingitis that the diagnosis is first made through microscopic examination, and comes as a matter of surprise.

But in a certain number of cases the disease can be recognized by the naked eye. The most striking feature is the disposition of the fimbriae not to turn in or the infundibular opening to become closed. It is said that the fimbriated end of the tube remains open in about one half of the cases. The result is the escape of the infectious pus from the open tube into the abdominal cavity and the occurrence of a large number of peri-tubal abscesses surrounded by firm adhesions by which the pus is encapsulated, or if no such protection is afforded, by the presence of miliary tubercles upon the surface of the adjacent peritoneum.

Another feature is the frequent occurrence of very large pus tubes. Ordinary pus tubes are clavate or sausage-like, but in tuberculosis they are described as being retort-like, and have been known to contain as much as two litres of pus. Of course the visible presence of tubercles upon the exterior of the tube, or on its inner surface when opened, is significant and diagnostic. The lesions vary as

in all tuberculous disease but the frequent occurrence of nodular yellowish necrotic masses, and collections of cheesy pus here and there are fairly characteristic.

The microscopy of the lesion in no way differs from tuberculosis of other organs.

Cases of syphilis and actinomycosis of the tubes have occasionally been observed, but are so rare as not to merit special attention.

TUMORS OF THE FALLOPIAN TUBES

These are all rare. Nodular formations occurring in the recovery from salpingitis—salpingitis nodosa—must be excluded from the cases resembling fibroma and myoma. They occur near the uterine ostium, and in association with signs of salpingitis.

Leiomyoma is sometimes observed. It usually occurs in the form of small sessile or pedunculated nodules upon or in the wall of the tube.

Fibroma, lipoma, angioma, hemagioma and lymphangioma have been reported. Enchondroma and osteoma, also reported must be thought of with reference to the possibility of their being either metaplasias following the recovery of salpingitis, mixed tumors or embryomas.

The most important tumor is the primary carcinoma. Of it some 140 cases are on record. The diagnosis is perhaps impossible before operation. The tube is then found to be enlarged, and of a sausage shape, the chief increase being in the middle and outer thirds. The surface may be smooth and without signs of inflammation and even without adhesion to other viscera. When the tube is opened, it is found to be filled with a papillary and villous mass resembling that observed in cases of adeno-carcinoma of the body of the uterus, which the tumor resembles. But occasionally irregular more solid tumors are seen, difficult to classify, some undoubtedly carcinomas, and described as such, others less definite have been called endotheliomas.

Secondary carcinoma also occurs, the chief source being carcinoma of the ovary.

Sarcoma of the Fallopian tubes is apparently extremely rare. All cases appearing to be such should be carefully studied to determine whether they are not mixed tumors, teratoid tumors, or more simple tumors. The literature contains references to two cases each of round cell sarcoma and spindle cell sarcoma, one of myxo-sarcoma, one myo-sarcoma, one combined spindle and giant cell sarcoma, and three peritheliomas. (Frank.)

DISEASES OF THE OVARIES

Each ovary appears as a flattened ovoid, or almond-shaped organ varying from 2.5 to 5 cm. in length, 1.5 to 3 cm. in width and 0.5 to 1.5 cm. in thickness. It is proportionally very small in infancy, grows rapidly at puberty, but continues to increase in size up to about the 40th year, when the maximum size is usually attained. At any time, however, it may appear to be abnormally large

or small accordingly as it does or does not contain numerous small cysts result-
ing from the retrogression of atretic Graffian follicles. During the reproductive
period it may undergo temporary increases in size as the result of such physio-
logical activities as menstruation and sexual excitement.

In infancy the ovary is not only small, but is pink in color, soft in con-
sistency, and smooth upon the surface. In old age it again becomes relatively
small but is grayish or yellowish in color, hard, rough upon the surface, and
marked by many scars. At any period from infancy to senility it may contain
numerous small cysts—pin-head or pea size.

The outer surface is covered with a cuboidal epithelium which where perfect
and undisturbed may show cilia though ordinarily they are not seen. Below is a
rather indistinct fibrous capsule—tunica albuginea.

The substance is divisible into a cortex and a medulla, but they blend into
one another. The cortex is characterized by the presence of the primitive and
developing follicles, the medulla by their absence and by the presence of numer-
ous blood-vessels, which radiate from the hilum or point of entrance.

The general stroma of the ovary, consists of a connective tissue whose
extreme richness in elongate vesicular nuclei suggests that it is chiefly composed
of cells, though the cytoplasm of the cells is scarcely anywhere to be seen.
These cells indefinitely arranged in bundles, twist and turn aimlessly in all
directions. They are less closely approximated in the medulla, where inter-
mediate fibres occur in strands of varying thickness.

Imbedded in the cortex of the stroma are the primitive follicles containing
the unripe ovules or germinal cells. These are large cells with abundant cyto-
plasm and large nuclei, each containing a nucleolus. These cells lie singly in
the deeper portion of the cortex, each being surrounded by a single layer of
flattened cells resembling endothelium, but apparently only modified cells of the
stroma. As under certain circumstances, however, as will later be seen, they
behave differently from all other connective tissue cells, it may be that they are
essentially different in nature. Such primordial follicles are most numerous in
childhood, and diminish with increasing years, very few of them remaining
after the menopause. The most important histological modifications that occur
in the ovary result from circumstances attending the maturation of the germinal
cells and the associated changes in the ripened follicles, resulting in the forma-
tion of the *corpus luteum*.

Briefly the events are as follows: During the maturation of the ovum the
endothelial-like cells by which it is surrounded increase in size, become cuboidal
in shape, and multiply so as to form an increasing number of layers—the
stratum granulosum. The appearance of these cells and their subsequent
behavior is so definitely that of epithelium as to warrant the suggestion made
above that they are essentially different from the connective tissue from which
they appear to spring. About the time that the stratum granulosum arrives at
a stage of development three or four cells deep, the surrounding stroma also
begins to participate, and there appear in its fibrillar meshwork, large cells with
rounded ovoid nuclei, in increasing number, until quite a definite layer is formed
—the *theca interna*. As these increase, a certain amount of pressure seems to be

exerted upon the surrounding tissue which becomes condensed into a fibrillar
structure, the *theca externa*. The stratum granulosum greatly increases, form-
ing a bulky investiture for the ovum which, however, is rarely found, even at
this early stage, to be inclosed in a solid collection of cells. For as the cells of
the stratum granulosum reach a certain stage of development, the more cen-
trally situated begin to disappear by vacuolation, leaving a space filled with
clear fluid. At first this is irregular, then seems to be sickle-shaped, then
crescentic, finally spherical. At a point opposite to the external surface
of the ovary, the cells of the stratum granulosum remain heaped up into a
mound, the *discus proligerous* or *cumulus oöphorus*, near the center of which the
ovum lies surrounded by a mantle of cells, the *corona radiata*. The cells of
the latter are usually distinctly cylindrical in shape; the cells of the outer layer
of the stratum granulosum abutting upon the theca interna are frequently also
distinctly cylindrical, the cells elsewhere cuboidal. The cells of the theca
interna are separated from those of the stratum granulosum by a delicate
structure, the *glass membrane*, or *membrana hyalinosa*.

The number of primordial follicles contained in the ovary of infancy is
enormous, and has been estimated by Waldeyer as 100,000. Few of these are,
however, destined to mature, and by the time puberty arrives, they have been
reduced to perhaps less than a third. From puberty on many more die and dis-
appear, than mature, and as has been said, after the menopause very few remain,
though it is possible to find a few at almost any age.

What accident or circumstance determines which of the ovules shall ripen
and which follicles shall develop is not understood. Certain it is however, that
many embark upon the developmental process to suffer shipwreck en route, and
disappear. Such accident may befall at any point of development, retrogression
at once supervening, so that a great variety of appearances may be presented by
these *atretic follicles*, as they are called.

But in case the follicle does mature, and reaches a point corresponding
to what has already been described, its enlargement is followed by elevation
of the cortical substance covering it, gradual thinning of the elevated tissue, and
eventual rupture of this thinned surface, with the escape of the fluid contents
and the ripe ovum with it. This is called *ovulation* and is synchronous with
the advent of menstruation. At the time of menstruation, the ovary becomes
enlarged through active hyperemia, and its swelling may be a determining factor
in the rupture of the riper Graffian follicle it contains.

It now interests us to find out what follows the escape of the ovum, which we
leave to its fate.

But the subsequent fate of the ovum, in some mysterious manner determines
what will occur in the empty and apparently now useless follicle. In at least
99 cases out of 100 the ovum languishes and dies, upon which its follicle without
further increase in size, develops into a body described as the *corpus luteum of
menstruation*, that seems devoid of any function, and probably represents only
changes incidental to its own final disappearance, which proceeds slowly and
regularly.

If, on the other hand, the ovum becomes impregnated, then through some mechanism probably associated with the endocrine system, its follicle proceeds to enlarge greatly and to develop into a formation of epithelial gland-like appearance, in all probability a ductless gland.

Such a *corpus luteum of pregnancy* continues throughout that entire period, and for about a month thereafter. Between the corpus lutem of menstruation—the *spurious corpus luteum*—and that of pregnancy, the microscopic differences are not always such as to permit them to be definitely recognized. Their origin, formation, and termination are the same, but usually they differ in size as well as in duration.

When the ripe follicle distended by the cellular proliferation and fluid accumulation ruptures, the sudden relief of pressure usually results in laceration of some of the delicate capillaries of the theca externa, and hemorrhage into the follicular space. This is not invariable, and when it does occur, the quantity of escaped blood varies. Following the rupture and escape of the contents the follicle collapses, and its sides commonly fall together. The external laceration through the tunica albuginea, however, soon repairs, and the cavity of the follicle again becomes a closed space the center of which, irregular in shape, is more or less filled with follicular fluid, blood, and fibrin, which soon form a kind of jelly, in which filaments, red blood corpuscles, amorphus granular matter, and soon a few connective tissue cells can be recognized. If impregnation have not taken place, and the formation is to be a corpus luteum spuriosum, there follows a moderate increase of the granulosa cells, which usually remain separated from the sparse cells of the theca interna, by the hyaline membrane, so that a layer of some thickness, composed chiefly of granulosa cells, is thrown into folds, sections of which appear as a wavy layer interposed between the interior of the follicle and the ovarian stroma, from which it is separated by the thin vascular external theca. But if the ovum have been fertilized, the proliferation of the granulosa cells is much greater, and the cells of the theca interna also considerably increase in thickness, so that the cavity of the follicle becomes relatively less, and the cellular mass greater. It is then that the gland-like appearance develops. At an early period some of the granulosa cells begin to show the presence of yellowish granules of a lipoid substance called *lutein*. These increase as the cellular proliferation progresses, eventually being present in practically all of the granulosa cells, and in many of the thecal cells as well. Corpora lutea of menstruation may contain very few or none of the lutein cells, but the corpus luteum of pregnancy abounds with them, as though they were the proper secretion of that gland-like organ. A corpus luteum of pregnancy may reach a diameter of more than 2 cm. It is usually of prolate spheroidal form, and is apt to project from the surface of the ovary. The theca externa of these large corpora lutea always contains a large number of dilated small blood-vessels.

The lutein cells derived from the granulosa are very large, rich in cytoplasm, have relatively small vesicular nuclei that stain palely, and are filled with fine yellowish granules. Those derived from the theca interna are a little smaller,

have nuclei that stain more darkly, and contain relatively less of the yellowish granules so that they appear darker in stained sections.

It is usually taught that the lutein cells disappear through vacuolation, connective tissue growing in from the theca externa to replace them until the whole mass has become transformed into connective tissue which then becomes hyaline and eventually disappear through contraction. This seems to be a mistake. From the specimens that we have studied it seems as though the entire mass of gland-like cells slowly undergoes hyaline necrosis, with the formation of either a finely granular or actually hyaline formation whose size, morphology and distribution perfectly correspond with those of the epithelial portion of the gland. Such connective tissue as is present results from a slight proliferation of the connective tissue cells of the partitions resulting from the infoldings of the hyperplastic cell mass. Thus results the *corpus hyalinosum, corpus albicans* or *corpus candicans*, which through misunderstanding of its origin is also called the *corpus fibrosum.* The hyaline material is very slowly absorbed, probably through interstitial digestion, and as it disappears, the originally large hyaline body becomes thinner and smaller, until it becomes a small lobulated mass, more or less divided by ingrowing delicate strands of connective tissue cells, and finally is scarcely more than a wavy hyaline line.

During the period of sexual activity, follicles in all stages of maturation and corpora lutea in all stages of retrogression are apt to be present in the ovaries.

The retrogression, whether of the atretic follicles or of corpora lutea may be complicated by cystic change—i.e., distension with fluid. Whether this is to be looked upon as pathological is a question. Induration of the tunica albuginea, especially when it is supposed to follow peri-oophoritis is supposed to predispose to the condition by increasing the difficulty of follicular rupture.

CYSTS OF THE OVARY

Most of these have been considered in the section devoted to the "Congenital Conditions of Surgical Importance" to which the reader is now referred. But one of them, also congenital in origin, and resulting from the accidental inclusion in the ovary of fragments of the endometrial tissue, needs further mention. Whether in the normal environment of the body of the uterus, or in uterine fibroids—adeno-myomas—or in the ovary, or at the umbilicus, the endometrial tissue responds to the endocrine stimulus and at the appropriate time becomes hyperplastic and "menstruates." The resulting bloody accumulation must either be absorbed or accumulate. If the latter occurs in the ovary, a blood cyst—*chocolate cyst*—is formed. With each recurring period it increases in size, until it distends the surface tissues and ruptures.

It is possible that under these circumstances nothing important may result, but Sampson has recently shown that in many cases there follows irritation of the tissues receiving the discharged blood, notably Douglas' pouch, where dense adhesions form. But that seems not to be all. With the escaping blood there frequently go living fragments of the endometrial tissue which transported to a new environment become implanted and grow into masses resembling adenoma.

Microscopic examination of these dense adhesions following the rupture of the chocolate cysts usually show such adenomatous areas, and when the implantation is upon the body of the uterus, or upon the intestinal wall, the endometrial tissue grows with the occurrence of what to all intents and purposes resemble adeno-myomas.

Fig. 368.—Dermoid cyst of ovary, showing sebaceous material and hair. (*MacCallum.*)

In a later paper Sampson expresses the opinion that the endometrial cells may reach the ovary primarily from the uterus or from the tube in internal menstruation, and that from such cells ovarian endometrial hematomas may arise. He also believes it possible that implantation adenomas of similar kind may arise without the intermediation of the ovary as an incubating organ, directly from the tube, from cells of the uterus or tube.

TUMORS OF THE OVARY

If one exclude the teratoid tumors, the dermoids, the mixed tumors, and the very rare simple tissue tumors which can usually easily be diagnosticated, there remain a considerable number of tumors malignant in disposition and extremely difficult of microscopic differential diagnosis that are included under the *carcinomas* and *sarcomas*. It is fortunate that both are malignant and that therefore the treatment is either case is the same. It is also fortunate that the diagnosis is usually reserved until the tumors have been operatively removed, so that the further treatment of the case does not depend upon the diagnosis. Thus the

matter of correctly classifying them becomes of academic interest only. A certain number sufficiently correspond with the accepted histological structure of carcinoma to be readily assigned to that class; others, distinctly composed of round or spindle cells are readily assigned to the class sarcoma, and with these

FIG. 369.—Teratomatous cystoma of the ovary, containing teeth and a tongue-like structure covered with hair. (*MacCallum.*)

diagnoses most pathologists and surgeons will be satisfied. But a relatively large number cannot be classified to any one's satisfaction. They may be either carcinoma or sarcoma. We have already expressed the opinion that it is a mistake to suppose that every malignant tumor must be either a carcinoma or a sarcoma. These tumors conform to the requirements of both, or sometimes to neither. They have also been described as endotheliomas but the suspicion must always be aroused that this diagnosis is but a subterfuge by which to overcome the difficulty just pointed out.

THE ALIMENTARY TRACT
THE MOUTH

Squamous cell carcinoma of the mouth most frequently occurs at the middle of the lower lip, the postero-lateral aspect of the tongue, the alveolar borders, upon the soft palate, and in the tonsil. In all cases it is more frequent in men than in women.

Upon the lip, the disease is visible to the patient and perhaps on that account may come very early under observation, and the earlier it does so, the greater is the difficulty of making a correct diagnosis. The usual first appearance seems to be that of a small firm papule upon the modified skin at the lip margin. It may be no larger than a pin's head, and in the course of weeks or even months, may not have increased beyond that of a half pea. It is not sensitive, and causes no particular annoyance. It slowly grows larger, and then begins to show a central ulceration of the surface. Sometimes it assumes a more papillary form, looks like a wart and is hard. In either case it is a suspicious lesion but a correct diagnosis may not be possible without the aid of the microscope.

But as at this early period the excision of the fragment for examination can be peformed under local anaesthesia, and as the removal of a cancer of such small size is frequently followed by cure, it is just as well to remove a wedge of tissue including the entire thickness of the lip, and leaving a generous margin of healthy tissue on both sides, so that if the suspicion of malignancy prove to be justified, the actual excision of the tumor is effected. It may be possible to completely destroy such a small carcinoma by fulguration with the electric spark, or with radium. If the tumor have developed to about the size of a soup-bean, and exhibits a red superficial ulceration, although its margins are indurated, and purplish in color, it may be mistaken for a syphilitic chancre. As, however, cancer of the lip is common, and chancre rare, the latter diagnosis should only be made with caution. Examination of expressed fluid by means of a dark-field illuminator, for the presence of Treponemata should be tried. Tumors of this size usually have invaded the sub-mental or sub-maxillary lymph nodes, and simple excision may fail to cure them. It is recommended in such cases not only to remove the tumor together with a generous amount of the adjacent lip tissue, but also at the same time to remove the lymph-nodes on both sides. A considerable number of cases are never heard from after this treatment. The larger the tumor grows, the more difficult its thorough eradication becomes, because of its local extensions and its metastases. The two do not progress uniformly. Some cases tend to spread locally, especially when infected so that the tissue of the lip swells and affords easy dissemination of the tumor cells, to the corner of the mouth or even to the cheek, and through its later necrosis and ulceration effect great disfigurement as well as open the path to extensive infections and hemorrhages. On the other hand, the tumor may early invade the lymph nodes, and give rise to secondary tumors in the neck, eventually extending into the chest and to the lungs.

Such carcinomas as arise in the tongue, also of the squamous cell variety, are usually to be found along a lateral edge, and near the base, but may occur anywhere. Most frequently they are at a position where the tongue is cut and irritated by a sharp carious tooth. The invasion of the soft tissues by the extending cancer growth takes place rapidly as does metastasis to the lymphatics. On this account the mere excision of the tumor never succeeds in preventing its return, and associated excision of the tumor and eradication of the associated lymph-nodes, no matter how thoroughly and how early performed is sooner or later followed by return. The disease is highly destructive locally,

causing extensive ulcerations, infections and sloughs, followed by enlargement of the lymph-nodes, attachment to the skin, necrosis and ulceration with external opening and discharge, followed frequently by hemorrhage, further infection, cachexia, weakness, and eventual death, either from hemorrhage or the weakness following repeated hemorrhage, or from inhalation pneumonia.

Irradiation by X-rays or radium prior to careful and thorough eradication of the cancer, and the removal of the associated lymph-nodes, whether invaded or not, and subsequent irradiation with X-rays at not too long intervals, is recommended, as affording the best hope for the patient. Some pin their faith to frequent fulguration with the electric spark, by which the cancer tissue is gradually destroyed. But both of these methods of treatment are too new for accurate comparisons to be drawn between them and the more purely surgical methods. No matter what treatment is pursued, the disease usually returns, and eventually causes death unless some intercurrent affection carry off the patient.

The squamous cell carcinoma of the alveolar processes is a variety of malignant epulis in most cases, and presents the complication of early bone invasion. The palatal and tonsillar squamous cell carcinomas rarely come under observation until they have formed fair sized crateriform ulcerations with purplish indurated borders sufficiently characteristic to need little assistance in diagnosis. They are locally destructive and invasive, extend to the associated regional lymph-nodes, and may be followed by the train of successive evils described above.

Lymphangioma, *hemangioma*, and *benign tumors* frequently occur at the points indicated, but are sufficiently characteristic to require no special mention. The reader is referred to the sections upon Tumors, and upon the Congenital Conditions for particulars.

Concerning the *epuli*, however, it seems necessary to remark that it may be impossible to determine the structure of a tumor arising from the gum until a microscopic examination is made. It is then found to be fibrous, when it is usually definitely benign, epitheliomatous—squamous cell carcinoma—when it is definitely malignant, or sarcomatous—usually of the giant cell variety— when it may be either benign or malignant, probably more frequently the former. However, the epulic giant cell sarcomas sometimes deeply invade the bone through the tooth follicles, enter the marrow cavity, where they effect extensive destruction, or necessitate extensive tissue removal in order to eradicate them. Spindle cell epuli behave irregularly; some are not subsequently heard from after removal, others persistently recur like other spindle cell sarcomas.

The various cysts of the mouth are fully described in the sections upon Congenital Conditions, and upon Cysts.

THE ESOPHAGUS

In the posterior wall of the esophagus, at the level of the cricoid cartilage, there is usually a slight depression called the pharyngo-esophageal dimple.

It marks the point at which the esophagus and pharynx join, and at which the arrangement of the muscle tissue occasions a slight weakness.

At that point too, the expansion of the esophagus anteriorly, as food passes through it, is prevented by the cricoid cartilage. In rare individuals, after middle life, this point seems to suffer from some separation of the muscle fibres, so that the mucous membrane undergoes hernial protrusion at the time a bolus of food is swallowed. This pressure may so develop, and the consequent hernial protrusion assume such proportions that a sac is formed, the *pressure or pulsion diverticulum of the esophagus.*

The frequency of this is unknown, as it does not always produce serious symptoms, nor is it always recognized when it does. In severe cases, i.e., those in which the sac becomes large, it begins to receive food as swallowing begins, and with each mouthful receives an addition until it is distended into a pyriform receptacle as large as a small pear. This, unable to project posteriorly because of the resistence of the spinal column, usually turns outward to the left. As it becomes filled, its lower part presses upon the esophagus between it and the trachea, compressing it, and causing increasing dysphagia until nothing can any longer be swallowed. The patient therefore scarcely receives more than the first few mouthfuls of his food, and gradually emaciates, until, as in a case studied by me, at autopsy, he actually starves to death.

FIG. 370.—Large pulsion diverticulum of the esophagus. Lateral view. (*After Zenker.*)

The larger sacs when full can usually be felt in the side of the neck, and may be emptied by pressure, the contents then regurgitating. If not emptied, the food is retained for a considerable time during which it undergoes chemical changes of putrefactive nature, which cause irritation and unpleasant eructations. It will be seen that the chief trouble is mechanical obstruction; also that the nature of the obstruction may be difficult to determine. In the case above referred to, no correct diagnosis was reached, and the patient starved to death. In order to explore the esophagus, bougies were introduced, and sometimes they found their way into the stomach, at others they went into the diverticulum and could not be persuaded to go further. It was supposed that the man had an esophageal cancer with various passages, through one of which the sound passed, and through which fluid could usually be swallowed. That was before the use of the X-rays. If he had been given a bismuth mixture, its accumulation in the neck in the pyriform sac would at least have suggested the nature of the difficulty. Judd, from a study of 200 cases, of which 54 were from the Mayo Clinic, finds this method of making the diag-

nosis rarely attended by difficulty, though it may not be easy to differentiate diverticulum from other varieties of esophageal obstruction, as, for example, those arising from cardiaspasm and from cancer. Once the nature of the condition is known, it seems not to be difficult to treat it by excising the sac through an incision in the side of the neck, and out of Judd's 54 cases there were only 3 deaths, and only one recurrence. All of the other patients recovered functionally as well as physically.

FIG. 371.—Diverticulum of esophagus, from skiagraph. (*Plummer.*)

A second, much more rare seat of pressure diverticulum is at the lower part of the tube, just above the bifurcation of the trachea. It is commonly spoken of as the epibronchial diverticulum. In a few cases pressure diverticula have been seen just above the diaphragm, and very occasionally they occur at other points. Fortunately these diverticula are of comparatively small size and trivial importance as their position precludes operative treatment. The so-called *traction diverticula*, caused by the tugging of the adjacent viscera upon esophageal adhesions, are almost always very small, have their lumina directed upwards, are, in consequence, seldom enlarged by the pressure of the passing food, and have no positive surgical interest.

Carcinoma of the esophagus is of common occurrence, the seats of predilection being the lower third, and more rarely the upper third. In the former the disease seems to begin on the anterior wall, not far from the point of bifurcation of the trachea; in the latter, near the cricoid cartilage.

The gastro-esophageal junction is easy to recognize as the esophageal mucosa is pearly and smooth, while the gastric mucosa is pinkish gray and velvety.

But the junction rarely forms a clean-cut line; instead, there is a more or less serrated irregular line of junction, and islands of the gastric mucosa may sometimes be observed in the esophageal tissue, or of the esophageal tissue in the gastric mucosa. When the tumor occurs close to the junction, it may be difficult to determine accurately from which tissue it actually begins. The histological structure of the tumor, however, usually makes this clear, as the typical esophageal carcinoma is of the squamous cell variety. But occasional tumors chiefly situated in the esophagus are of the columar cell type, and occa-
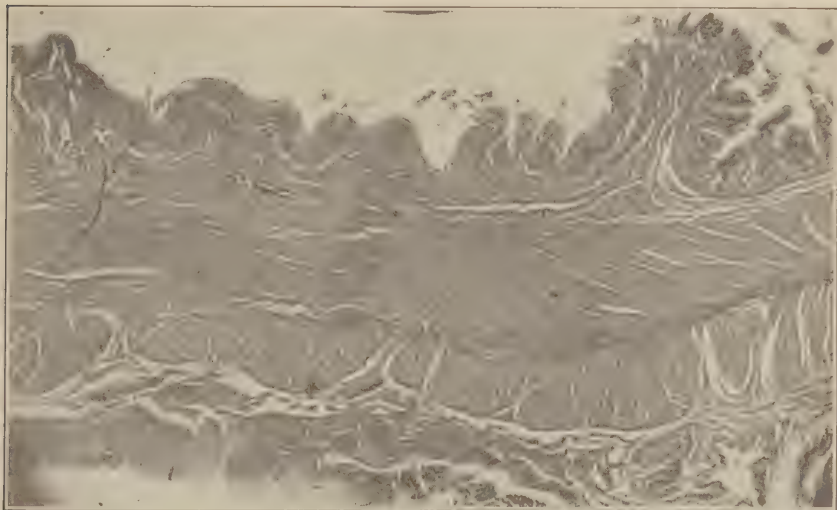
FIG. 372.—A plaque of squamous epithelium in the gastric mucosa. The normal cylindrical epithelium of the part can be distinctly seen, thrown into folds, at the extreme upper right hand part of the illustration. A coarse elevation separates it from the squamous stratified epithelium that covers all of the remainder and stops again just to the left of the field shown. (*From a photomicrograph by Prof. Allen J. Smith.*)

sional tumors of the stomach are of the squamous cell variety. Such are supposed to arise from dislocated fragments of the respective gastric or esophageal mucosae. The tumors that arise higher in the lower third, and presumably all of those occurring in the upper third are squamous cell tumors.

The form assumed by the tumors varies. In some cases the growth is slow and annular with added formation of cicatricial connective tissue, so as to justify the term scirrhus. The esophagus is constricted and obstructed. Increasing dysphagia, may be the only symptom of which the patient complains. In other cases the tumors assume the form of more or less circular plaques with ulcerated centers and indurated edges. These may exist for a long time without giving important symptoms, as little obstruction is effected. But the most frequent form observed is an annular growth which infiltrates the wall of the tube, at the same time that large masses are formed in its interior. In such cases obstruction is caused by the double effect of the presence of the masses which act mechanically and the infiltration of the wall which destroys its distensibility. The swallowed food caught in the obstructed passage, collects,

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undergoes putrefaction through the agency of bacteria, and acts as a constant source of irritation by which necrosis of the tumor tissue is facilitated. Under these circumstances the lower part of the esophagus fills up with an irregular mass of necrotic and sloughing tumor tissue. Above the obstruction the tube dilates, and its wall hypertrophies, so that a sac forms, in which the swallowed

FIG. 373.   FIG. 374.

FIG. 373.—Squamous-cell carcinoma of the esophagus. *a*, Epiglottis; *b*, larynx; *c*, dilated esophagus with the posterior wall pressed forward by enlarged lymph-glands; *d*, enormous degenerating tumor-mass through which a very small channel permitted food to enter the stomach; *e*, aorta.

FIG. 374.—Carcinoma of upper end of esophagus. (*From a specimen in the Pathological Museum of the University of Pennsylvania.*)

food collects, to be subsequently regurgitated, in many cases. In such cases, attempts to arrive at the diagnosis with the aid of an esophageal sound, may be disastrous as pressure upon the softened tumor tissue occasionally results in false passages with later infection of the mediastinum, pleura, or pericardium. The

progress of the disease varied in different cases. Sometimes it remained confined to the wall of the esophagus, sometimes it grows down to and invades the wall of the stomach, sometimes it quickly spreads to the lymphatics. But in ordinary cases the infiltrated esophageal wall eventually undergoes the same necrotic change as the internal tumor masses, and is resolved into a pultaceous

mass, that sooner or later ruptures into neighboring cavities or effects communications with adjacent viscera. The most frequent perforation seems to be into the respiratory tract. In the Museum of the Post Graduate School of the University of Pennsylvania there are two such specimens, in one the oesophagus had ruptured into the right bronchus, in the other into the left. In each case the patient had died of pulmonary gangrene, with more or less extensive septic pneumonia. But the perforation may effect communication with the pleura, the pericardium, or the mediastinum. Perforation of the aorta has been known to follow adhesion to its tissue, with invasion and weakening. In nearly all cases there is more or less invasion of the lymphatic nodes of the mediastinum. Secondary nodules may occur in the lungs and liver, but are not invariable. Where false passages are effected by careless sounding with the esophageal bougie, unexpected dis-

FIG. 375.—A pedunculated lipoma of the esophagus protruding from the mouth (*Vinson.*)

tribution of the morbid effects may be observed, as in a case reported by B. Fischer, who performed an autopsy upon a patient in whom the sound had passed through the wall of the esophagus, through the diaphragm, and perforated the entire left lobe of the liver, with the result that the swallowed food passed directly into the abdominal cavity.

As has been said, the tumors are usually frank squamous cell carcinomas, but occasionally one is surprised to find an appearance suggesting carcinoma rotundo-cellulare, and in rare instances columnar cell tumors have been encountered.

No surgical treatment has thus far proved to be of benefit, partly because of the inaccessibility of the diseased tissue, and partly because of the fact that the diagnosis can only be made late in most cases, even now when the X-rays and barium meal enable one to see what goes on when the food is swallowed. The patients die either from infection and phlegmonous infiltration of the mediastinum, from pleurisy, pericarditis, atrophy from inability to get the food into the stomach, or from hemorrhage. Probably the most frequent cause of

death is septic pneumonia and gangrene of the lung after perforation of the bronchus.

Benign tumors of the esophagus are rare. They have the same general distribution as the cancers, that is, arise for the most part from the anterior surface of the lower third, or from the posterior aspect of the upper third. All of these tumors are peculiar and on account of their rarity not much is known about them. Undoubtedly some of them are or arise from congenital defects, as, for example, cystic formations of the lower part, spaces in which are lined with columnar epithelium some of the cells of which are distinctly ciliated. There are also occasional rhabdomyomas that may be related to the mixed tumors. Both of these may have had their origin in early escape of the tissues of the esophagus from their normal position during embryonal development.

Mucous polyps, papillary fibromas and leiomyomas have been observed. Adenoma and cystic adenoma have been reported. Lipoma sometimes occurs. An interesting and peculiar case was operated upon by Judd and reported by Vinson. The patient, a man aged 62, upon vomiting, ejected from his mouth an elongated cylinder of tissue that projected 11.5 cm. beyond the incisor teeth, gradually tapered towards its base, was firm, and covered with normal mucous membrane. It was later removed through an incision in the side of the neck opening into the esophagus. It proved to be a pedunculated submucous lipoma arising at the level of the cricoid cartilage.

THE STOMACH

Peptic Ulcer

Certain peculiar ulcers, variously known as peptic, simple, round, benign and chronic, are found to be present in a little more than 1% of bodies examined at autopsy. If they occur in the same proportion among living persons, which is quite possible as their presence in the dead usually seems to be quite independent of the disease from which the patients died, every city of 1,000,000 inhabitants should presumably contain 10,000 individuals afflicted with them, and as cities of that size, in this country, average about 1,500 physicians each, if all of these patients were under treatment, there would be approximately 6 cases in the hands of every doctor all the time.

Such prevalence is not clinically recognized, however, not necessarily because gastric ulcer is not so common as the autopsy findings would indicate, but because many of those suffering from them experience no symptoms severe enough to warrant consulting a physician, and because the general vagueness of the symptoms is such that the condition commonly escapes diagnosis at the hands of practitioners who only see the patients occasionally. One should be alert to the probability that his patient with periodic or persistent dyspepsia may be suffering from gastric ulcer, lest he experience the chagrin of seeing him fall into the hands of some specialist who supplements his suspicion by an X-ray examination, and then confirms it by a surgical operation after which the indigestion of many years standing disappears.

When, because of the occurrence of hemorrhage or perforation the practitioner makes a positive diagnosis, much justifiable alarm is felt, for then surgical intervention may be the only remedy. But in the ordinary course of events the malady is not very dangerous, only 3.77% mortality from gastric ulcer being reported in 1191 cases. However, the disease is debilitating, disabling, chronic and may be fatal at any time, so that proper, and probably surgical treatment is indicated in all cases, as the mortality following operation is only 1.76%, and recovery after operation almost a certainty. If from these surgical statistics could be eliminated those cases with debility from long continued indigestion and frequent hemorrhages, as well as those in which the ulcer had already perforated, the death rate would be much lower, and the apparent benefits correspondingly greater.

FIG. 376.—Typical appearance of peptic ulcer of the stomach. Natural size. (*Photograph by Prof. Allen J. Smith.*)

It was formerly believed, and nearly all of the books state that peptic ulcer is most frequent in young women, and occurs only in the stomach, but the experiences of the Mayo Clinic, as reported in a paper upon "Gastric and Duodenal Ulcers" by Charles Mayo, show that peptic ulcer is more frequent in males, the proportion being three to one, and that duodenal ulcers are more frequent than gastric ulcers in the proportion of four to one.

Similar ulcers also occasionally occur in the lower part of the esophagus, in patients that suffer from acid eructations. They are, therefore, found in the lower part of the esophagus, the stomach, and the upper part of the duodenum, that is, in the distribution of acid secretion associated with pepsin. Upon rare occasions, after the performance of gastro-enterostomy, the entrance of acid gastric secretion into the jejunum is followed by peptic ulcer of that part of the intestine—gastro-jejunal ulcer. From this it seems as though there can be no doubt about the importance of the acid peptic secretions in bringing it about. But as the parts named are under normal conditions continually exposed to these secretions and are normally able to resist them, the occurrence of ulcer must depend upon some other abnormal condition. So long as the mucosa is normal, it is able to resist the digestive action of the gastric juice, but when diseased, may quickly be attacked. Ordinary traumatic injury does not destroy the tolerance, and operation wounds as well as accidental injuries inflicted by foreign bodies, heal perfectly and quickly. It must, therefore be some different and devitalizing influence that leads to peptic ulcer. Experience shows that when the gastric mucosa is the seat to inflammation, especially with abscess formation, the affected tissue is quickly attacked by the gastric juice, the infiltrated areas cleaned by digestion, after which the injury heals. In tuberculous and syphilitis lesions, the same is true so far as condi-

tions of similar character obtain. Thus, the tuberculous ulcer is fairly clean, though the borders may be the seat of tuberculous disease not yet attended by sufficient devitalization to submit to digestion. As the lesion spreads at its edges, the centre is continually being eroded by digestion.
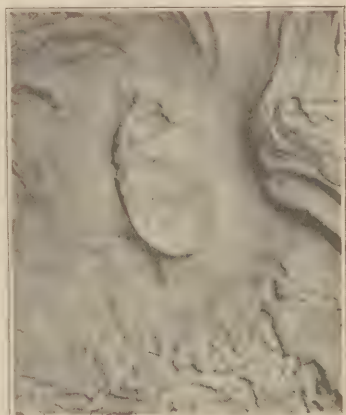
It would, therefore seem that the ulcerations must be caused by some condition by which circumscribed areas of the tissue are devitalized. What that condition is, is a matter by no means settled, and it may be no single condition,
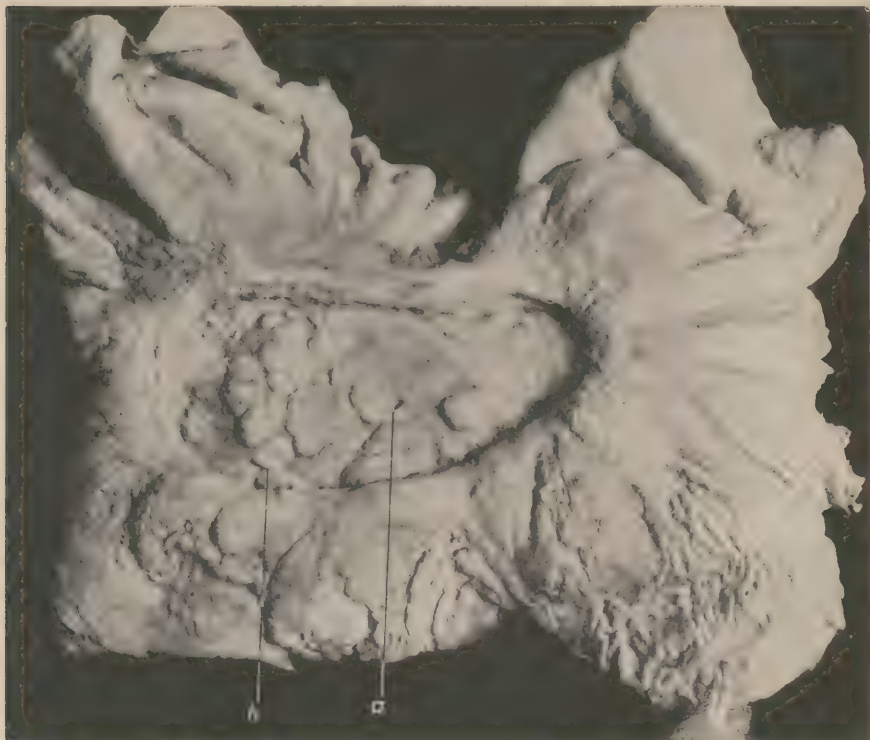
FIG. 377.—Large peptic ulcer of the stomach with perforation. ½ natural size. a, An eroded artery at the bottom of the ulcer; b, visible lobular structure of the pancreas to which the stomach is adherent, and which forms the base of the ulcer. (Johres.)

but any one of a number. Thus the lodgment of an embolus in one of the small vessels of the stomach or duodenum, on account of the arrangement of those vessels, may be quickly followed by ischemia and loss of the resisting power of the tissue which would quickly be digested away. Or, following embolism, thrombosis might accomplish the same result over a greater extent of the tissues. Rosenow has laid great emphasis upon the infectious nature of the lesions, and asserts that certain bacteria tend to colonize in the walls of the stomach, and that from the walls of peptic ulcers bacteria can be cultivated, which, when subsequently injected into the circulation of experiment animals, are found to colonize in their gastric walls with the production of ulcers.

But all attempts at the experimental production of gastric ulcer, fail to produce lesions corresponding with clinical gastro-duodenal ulcer, in that the experimental ulcers all tend to heal quickly, while the clinical lesions assume a remarkable chronicity, and may persist with very little change for as long as twenty years. Concerning the duration of the lesion however, there is no regularity. Ulcers are found in all stages of formation and regeneration, and enough

FIG. 378.—Gastric ulcer (round or peptic ulcer). (*MacCallum.*)

scars of antecedent ulcers are found to make it certain that many of them get entirely well, though the conditions that inhibit or facilitate healing are mysterious.

Very rare in the lower end of the esophagus, and unusual in the cardiac end of the stomach, the ulcers become generally speaking more numerous as the pyloris is approached, and are most numerous in the duodenum between the pyloric ring and the opening of the papilla of Vater. W. J. Mayo found that 534 ulcers out of 638 were located on or around the lower curvature. Of 85 ulcers of the posterior wall of the stomach 16.5% were in the cardiac third, 75.8% in the middle third and only 8.2% in the pyloric third. There may be one, they may be paired, symmetrically situated upon opposite sides of the pyloric opening, or there may be many scattered about irregularly. In Mayo's series of 838 cases 28 had multiple ulcers. In size they probably do not average more than a centimeter in diameter; some are much smaller, others much larger. Occasional peptic ulcers have been seen that were as large as a man's hand. The healing of large ulcers, sometimes results in great deformity of the organ, dividing it into pouches—hour-glass stomach.

The appearance of the ulcers is not uniform. Most frequent are "indolent ulcers," but even these vary according to their age, and probably according to

the method of formation. According to the classical description the peptic ulcer is well rounded, slightly ovoid, and cleanly and sharply edged as though the tissue of the gastric wall had been "cut out with a punch." Its edges are not infiltrated, and there are no associated signs of inflammation. It is not the molecular tissue destruction following suppuration as is an ordinary ulcer, but the cleanly removal of necrotic tissue by the digestive fluids.

FIG. 379.—Roentgenogram showing the Reiche-Handek niche of gastric ulcer. (*Carman.*)

The ulcers extend to various depths. They may involve the mucosa, or descend through the submucosa, or on through the muscularis mucosa, or even through the muscularis, and have only the serous coat for the base. They may even penetrate the serosa, when, of course they perforate—one of the most serious accidents of peptic ulcer. The ulcers that involve several coats, may have the same clear sharp margins and punched out appearance, or may show "terraces" as they descend through different coats one after another. The terracing may be concentric and regular, but is perhaps more apt to be eccentric.

Ordinarily the edge of the ulcer is not infiltrated or elevated, but it may be, and is then supposed to indicate either that it is in a formative stage, or is beginning regeneration. At the bottom of some peptic ulcers, especially the deep and eccentrically terraced ones, a red point may be seen. This may be immediately recognizable as a small blood-vessel, or prove to be such upon later investigation. Such a vessel is apt to be thrombosed, and some have supposed

its obstruction to be the cause of the ulcer. As, however, the occasional extension of an ulcer erodes an artery and permits hemorrhage varying from a few drops of blood to massive and even fatal hemorrhage, it seems rather as though the ulcer was the cause of the exposure and thrombosis than the reverse.

The partial destruction of the gastric wall naturally results in local weakening which permits bulging when there is internal pressure. This permits the easy recognition of such ulcers as are so situated as to be observable in profile by the X-rays after the ingestion of barium milk. The greater the depth of the ulcer, the more it will bulge. Prolonged bulging followed by healing may result in short diverticula.

It would seem as though some ulcers begin to heal soon after formation, while others gradually extend. Ulcers known to have been in existence for a long time sometimes occasion hemorrhage or perforate which they could not do if they did not extend to new tissue. Fortunately such untoward events are rare, and death from gastric ulcer occurs only in about 3.77% of the cases. Ulcers posteriorly situated, if very deep and liable to perforate, become adherent to adjacent viscera, so that by the time the perforation is effected, the opening is closed and the contents of the stomach unable to escape into the abdominal cavity. Ulcers anteriorly situated may not be able thus to prepare for the accident which is followed by fatal peritonitis unless operative intervention can be immediately supplied.

Adhesion to the viscera, however, does not prevent all future damage. The digestive juices are brought into contact with new tissues not qualified by nature to resist them, and gradually erode them with the formation of pockets of increasing size and inflammatory surroundings which embrace more or less of the pancreas, the liver, the spleen or other viscera. Chronic cicatrization, more or less circumscribed suppuration, or phlegmonous inflammation of the surrounding parts with sub-phrenic abscess or diffused peritonitis may thus be brought about. Perforations have been known to open the gall bladder, the pleura, the pericardium, the portal vein and the pelvis of the kidney.

The scar following the healing of peptic ulcer is usually dense and puckered. Surgeons frequently speak of partly cicatrized ulcers as *callous*, and such cases are commonly regarded as chronic.

Mayo attributes the preponderance of males over females with duodenal ulcer to anatomic reasons. He says, "In the female the first part of the duodenum is more nearly transverse than in the male, so that the alkaline juices of the bile and pancreatic secretion more or less constantly bathe the upper duodenum. In the average male, the first part of the duodenum, as a rule, passes upward, and then the second portion, to the common duct, descends so that the first inch and a half of the duodenum is not so readily alkalinized."

Considerable apprehension is always expressed concerning the possibility of carcinoma developing from gastric ulcer. The bases and sometimes the margins of these ulcers when examined microscopically show carcinomatous tissue, although to the naked eye the ulcer does not differ from simple ulcer.

This is subject to two different interpretations: first that the carcinoma is somehow engrafted upon or is developing from the ulcer; second, that a small

carcinoma has been attacked by the gastric juice and destroyed to an extent that leaves scarcely any but healthy tissues remaining. At the present moment we are not in a position either to avow or to deny that carcinoma develops from ulcer. If it does, it does so much more frequently in the stomach than in the duodenum, though duodenal ulcers are more frequent.

Cancer of the Stomach

Cancer of the stomach comprises about one third of all cancer cases. It is more frequent in men than in women, the proportion being roughly about 2:1. It occurs at almost all ages, but is most frequent in the sixth decade of life. Eighty two per cent of all cases occur between 40 and 70 years of age. Thirty-three per cent occur between the 50th and 60th years.

By far the greatest number of tumors occur in the pyloric third of the stomach, a relatively small number in the middle third, and a very few in the cardiac third. Of those in the pyloric region the greater number are situated near the pyloric ring, arising from the lesser curvature of the posterior wall. For some reason not known the tumors confine themselves to the stomach, and do not pass through the pyloric ring into the duodenum. The rapidity of growth varies greatly, without reference to the type of structure. In general soft infiltrating carcinomas are more rapidly fatal than hard scirrhus ones.

The actual duration of such a tumor cannot be accurately determined as it exists for some time before symptoms develop. Indeed it is not unusual to find a cancer of the stomach at autopsy upon a patient dead from some other disease, in whose history no symptoms suggested the presence of the tumor.

From the time that symptoms are manifested the duration of life varies from three months in the so-called acute cases, to two or three years in chronic cases.

The tumor presents several strikingly different appearances:

1. *Pyloric Scirrhus.*—This occurs as a hard obstructive induration about the pyloris which slowly contracts, and prevents the food from escaping into the duodenum. Associated with it there may be a larger or smaller ulceration near the pyloris. Upon microscopic examination such a tumor usually appears as carcinoma rotundocellulare, with much dense connective tissue matrix and small cell nests. It obstructs the pyloric outlet, and causes a great dilatation of the stomach, whose walls first hypertrophy, then being unable to compensate beyond a certain point, stretch, so that the stomach dilates to an enormous size and descends, first toward the umbilicus, and then toward the pubis as its weight becomes increased through retained contents.

2. *Leather-bottle Stomach.*—This is a diffuse form of scirrhus, not limited to the pyloric region, but fairly uniformly distributed throughout the entire wall of the organ. Its effect it to reduce the organ to a small size, and greatly increase the thickness of its walls which become tough and leathery, creak as the knife cuts them, yet shown no localized or distinct tumor, so that many have supposed the condition to be the result of a chronic form of inflammation. It is conceivable that chronic inflammation may have such an effect,

but the examination of the tissues shows carcinoma in practically every case. Ordinarily there are no, or few ulcerations. It is a comparatively rare variety of gastric carcinoma.

3. *Soft Ulcerated Fungus Carcinoma.*—This is by far the most frequent form of carcinoma of the stomach. It occurs as a distinct and fairly well circumscribed tumor situated near the pyloris, commonly on the posterior wall and upon the lesser curvature. Its size, of course varies according to its age, up to the formation of a mass as large as a man's fist. It is nodular and irregular, soft in consistency, pinkish in color, rounded at the margins which are apt to

FIG. 380.—Section through a stomach, the walls of which are diffusely infiltrated with carcinoma. The organ is contracted and its walls are greatly thickened—"leather bottle stomach." (*Bowlby and Andrewes.*)

over-hang thus giving it its fungous character. In almost all cases the center is ulcerated and forms a crater sometimes deep and circumscribed, sometimes, and probably more frequently broad and more superficial. It trespasses upon the pyloris which is partly obstructed, so that it produces, but to a more limited extent, the hypertrophy, dilatation and dislocation described under scirrhus.

When examined microscopically it usually proves to be carcinoma cylindrocellulare, in which the glandular structure is frequently remarkably well preserved. It is such tumors that form the groups described as malignant adenoma and adeno-carcinoma.

4. *Gelatinous Carcinoma.*—This mucoid, mucinoid or colloid variety of carcinoma is probably more frequent in the stomach than in any other organ. It is striking in its softness, and in the abundant collections of mucilaginous material contained in its spaces, which frequently resemble cysts and sometimes actually form such. In some cases so much cell transformation has taken place that most of the tumor tissue seems to have been replaced by jelly-like accumulations. These are variously grayish and opaque, or yellowish and transparent,

sometimes as clear and transparent as calves foot jelly or culture gelatine. What appear to be vesicles filled with such material sometimes occur upon the exterior of the stomach, about the pyloris and lesser curvature, where the lymph nodes are located, and represent the transformation of the secondary deposits in these nodes into the jelly. This intimates what will be found before the stomach is opened for examination.

FIG. 381.—Roentgenogram of malignant saddle ulcer in the pyloric end of the stomach. Irregularity of the greater curvature opposite the ulcer is due to spasm. Note the concavity of the meniscus toward the gastric wall. (*Carman.*)

Upon microscopic examination it will be found that the mucinoid carcinoma has no other characteristic features than its peculiar degeneration, and may be carcinoma rotundo-cellulare or carcinoma cylindro-cellulare.

5. *Squamous Cell Carcinoma.*—This is extremely rare, and is almost invariably situated at the cardiac end of the stomach, where it is supposed to arise from tissue associated with the esophageal insertion. It takes the form of single or multiple flattened discs that ulcerate. Annular deposits about the esophageal entrance may effect obstruction of that tube and marked dysphagia. Under these circumstances it is the esophagus that hypertrophies and dilates, the stomach becoming smaller as the food finds it more and more difficult to enter.

The ill-effects arising from the cancer are partly chemical and physiological and partly mechanical and anatomical. In most, but not all gastric cancers there is a gradual loss of the free hydrochloric acid from the gastric juice. Just

how this is effected is obscure. The total acids seem not to diminish, though the free acid does. The cases in which the disappearance is most marked are almost always those with large ulcerating tumors, hence is seems as though the condition might be local and dependent upon some kind of combination between the necrotic tumor mass and the acid, by which a greater than normal quantity of the hydrochloric acid becomes fixed. This loss of acid interferes with digestion, permits putrefactive changes to take place in the retained food, and permits the carbohydrates to undergo lactic acid fermentation the irritative effects of which lead to increased destruction of the carcinoma tissue. These accumulated morbid products also occasion much of the vomiting from which the patient suffers, and which causes the loss of much of the food the patient takes, so that emaciation is usually rapid. In cases that do not vomit, the absorption of the morbid products are equally injurious. The continued acidity also tends to prevent the opening of the pyloric orifice and the continued retention of food in the stomach where conditions of digestion are diminished.

The mechanical and anatomical effects result from the obstruction at the pyloris, and the loss of the contractile power of the wall of the stomach infiltration by the tumor, its dilatation and dislocation.

It will be seen that from these points of view those patients will do best and, other things being even, will live longest in whose stomachs there are no pyloric obstructions and no ulcerated cancer masses. This is indeed true for the cases of leather-bottle stomach, and squamous cell carcinoma of the cardiac end live longest.

But in all cancers other factors come into play to modify and interrupt the course of events. Thus, there are the accidents of hemorrhage and perforation. Every gastric cancer, to all intents and purposes, is or soon becomes a peptic ulcer. In the natural course of events the cancer shows its customary disposition to ulcerate, the gastric juice then eroding away the diseased tissue, precisely as in peptic ulcer without cancer. If there be no loss of the free hydrochloric acid, this erosion is rapid and keeps pace with the growth of the tumor and its necrosis. Sometimes the erosion is so complete as to leave the ulcer so flat and clean as to make it difficult to recognize as cancer, and it will be remembered that in discussing the peptic ulcer it was pointed out that in many cases it was first suggested that the lesion was cancer only after the microscopic examination was made. There are no doubt not a few cases in which even with the aid of the microscope the cancer elements are not found, and the lesion passes for a simple ulcer although really carcinoma. Thus is explained the discouraging fact that many cases operated upon by the surgeons for ulcer, and supposed to be cured, later die of carcinoma of the stomach—a circumstance not infrequently probably misconstrued to mean that a simple ulcer subsequently became cancerous. Being, then potentially a peptic ulcer, the cancer may suffer peptic destruction of some part of its tissue containing a blood-vessel, and hemorrhage may occur.

Indeed, hemorrhage is so frequent a symptom of carcinoma of the stomach that it is always looked for and expected, not without justification. The blood may find its way into the intestine where it appears as occult blood

in the feces, or it may be vomited, either as fresh and bright blood, or as coagulated partly digested blood according as it is acted upon and partly destroyed by the fluids in the stomach. In the latter case it may present the appearance described as "coffee-ground vomitus."

If the erosion effected be deeper, perforation of the gastric wall may occur, under conditions almost exactly parallelling those of peptic ulcer. That is, before the perforation is completed, adhesions may form between the wall of the stomach and neighboring viscera.

But of greater importance than these accidents, is that peculiar to malignant tumors, and giving them one of their chief dangers, namely *metastasis*. The conditions under which this may take place cannot be predicted. Some cancers grow to considerable size before metastasis takes place, others show it so early that the patient dies of the metastasis before the primary lesion seriously disturbs him. The distribution of the cancer cells follows the usual rule. The first secondary lesions are almost always to be found in the lymph-nodes in the neighborhood of the pyloris and about the lesser curvature. Following them, and occasionally without them the cells find their way to the liver, and it is there that the greatest tumor masses develop. More rarely they reach the lungs, and in very rare cases the bones and other remote viscera.

Soon after the lymph nodes are invaded there seems to be a tendency for the peritoneum to become invaded, and this usually centers chiefly in the great omentum which sometimes becomes transformed into a thick and solid cancerous mass that may have an extent as great as two spread-out human hands and a thickness of several inches. Occasionally either through lymphatic extension or as the result of the admission of free cancer cells to the peritoneal cavity, small carcinoma nodes may be distributed over almost the entire peritoneum—*carcinomatosis peritonei*. That this may result from the presence of free carcinoma cells seems to be indicated by the not infrequent localization of the nodules in the most dependent part of the peritoneal cavity, the pelvis. In some cases the tumor invades the veins, first those draining the stomach, then the portal vein, which becomes thrombosed, and eventually conducts the cancer cells to the liver.

The growth of the cancer in the stomach itself varies. In some cases it is slow, and attended by the formation of much dense cicatricial tissue, so that the scirrhus of the pyloris is brought about. In others it grows more rapidly so as to form a great soft fungous mass. In still others it almost immediately begins to infiltrate the wall of the stomach, either widely and diffusely so as to produce the leather-bottle stomach, or locally so as to penetrate the entire thickness of the wall of the organ below its chief seat.

The surgical treatment of carcinoma of the stomach is subject to the usual limitations. In the hope of effecting a cure it should not be undertaken except in very early cases, and before the regional lymph-nodes are involved. The following table constructed from the statistics of MacCarthy and Mahle, and based upon the microscopical study of the material from 200 resected stomachs, indicates the difference in the duration of life made by the presence or absence of lymphatic metastasis in cancer of the stomach.

Patient lived, years	Lymph-nodes not involved, per cent	Lymph-nodes involved	
		Nodes of lesser curvature near pyloris, few in number, alone involved, per cent	Many nodes on both curvatures about pyloris involved, per cent
1	78.8	50.0	50
2	60.0	21.4	30
4	33.0	8.9	20
6	21.0	5.3	10
8	12.0	3.5	10
10	6.0	0.0	0
11	2.0	0.0	0
13	1.0	0.0	0

But apart from the hope of effecting a cure and increasing the expectation of life, there seems to be another good reason for operating upon such cases of carcinoma of the stomach as are not in such condition from the formation of adhesions etc. to make it impossible. It is to rid the patients of the mass of necrotic sloughing material that is a source of obstruction, of frequent hemorrhage, and of occasional deep ulceration, and whose putrefaction is the source of the fetor of the breath and the vomitus. Although he may not live many years longer, he becomes much more comfortable, better nourished, and more likely to die from carcinoma of the liver, which is less distressing, and unattended by the vomiting and starvation.

SARCOMA OF THE STOMACH

Primary sarcoma of the stomach is rare. Both round and spindle cell varieties have been described, but in many cases the study of the material seems to have been inadequate, and leaves one in doubt as to the exact nature of the tumor reported.

I. *Round Cell Sarcoma of the Stomach.*—Every tumor of the stomach appearing to be composed of round cells and suggesting sarcoma should be most carefully studied to make sure that it is not really a highly cellular carcinoma with anaplastic cells. This caution is based upon the fact that not a few of the cases reported as sarcomas have borne a general resemblance to carcinoma, ulcerated, invaded the lymph-nodes, and involved the omentum and peritoneum as carcinoma does. Also upon the statement made by certain authors that the particular tumors reported by them were partly carcinoma, and partly sarcoma. Carcinoma may be so cellular, and its cells so modified in size and appearance as to resemble and be mistaken for sarcoma. The secondary tumor nodules in some cases of quite typical sarcoma are strikingly like carcinoma.

The most convincing cases of gastric sarcoma are composed of small round cells and commonly spoken of as *lympho-sarcoma*. They appear as larger or

smaller fungiform tumors without definite localization, arising in the submucosa, elevating the mucosa, which ulcerates, and occasionally invading the muscularis, though rarely destroying the entire gastric wall that may reach a thickness of 3 cm.

To the naked eye these tumors are nodular, soft, elastic, whitish or straw-colored, and uniform in structure unless hemorrhage or degeneration modify them.

They eventually cause metastasis to the regional lymph-nodes, to the liver, and to the omentum.

Broders and Mahle of the Mayo Clinic were able to collect 13 cases of gastric lympho-sarcoma from the literature, and to add 12 new ones from their services, so that there are now about 25 cases on record. In their experience the relative frequency to gastric carcinoma in 1:68. With one exception the patients were all males, the youngest being 16, and the oldest 62 years of age, the average 46 years. The patients were, for the most part, supposed to be suffering from either gastric ulcer or gastric carcinoma, and had been manifesting symptoms for an average duration of 6 months. Six of the cases were operated upon by gastric resection; six were inoperable. In general no benefit resulted from the operation.

When these tumors were examined with the microscope, they were found to be composed of round cells a little larger than lymphocytes, with vesicular nuclei showing single nucleoli, resembling those of the germinal centers of the lymph-nodes, though no germinal centers were found in the tumor structure.

It goes without saying that these tumors, formed no part of leukemia.

Leukemic nodules are not uncommon in the wall of the stomach, but are not here considered to be sarcomatous tumors.

II. *Spindle Cell Sarcoma.*—Here again care should be taken to examine enough of the tissue to prevent erroneous conclusion as to the nature of the tumor at hand. In other parts of the body, as has been pointed out, carcinoma cells occasionally assume a spindle shape. Leube has described a mixed sarcoma and carcinoma which Ewing refers to as showing that parts of carcinomas may give histological appearances resembling sarcoma.

The spindle cells composing these gastric tumors vary greatly in size and appearance in different cases. Some writers have supposed them to be the descendents of the involuntary muscle cells of the muscularis, and have called the tumors myo-sarcoma. But small spindle-cell, large spindle-cell, fibro-sarcoma, and myo-sarcoma have been reported. Both round and spindle cells are said to have occurred in different parts of the same tumor, in the case reported by Moser.

Some spindle cell sarcomas are small, others grow to be very large. One reported by Cantwell sprang from the posterior wall of the stomach of a woman and when removed weighed 12 pounds. In Baldy's case, the tumor rose from the greater part of the greater curvature and anterior and posterior walls, and filled nearly the entire abdomen of a man. When the tumors are small and first observed at autopsy, it is impossible to say how long they have existed or how they might have behaved. Those that come under clinical observation,

behave like sarcomas elsewhere, quickly return if removed and eventually destroy the patient.

If they arise from the outer layers of the gastric wall, they may grow more rapidly exteriorly, and project into the peritoneal cavity, as in Baldy's case; if they arise from the more internal layers, they may grow into and fill the gastric cavity. They may be solid, or cystic as the result of degeneration which gives a soft and gelatinous quality to their structure and frequently riddles them with cysts. Only the internal tumors are brought into contact with the gastric juice, hence only such ulcerate. The peritoneum is usually involved, and may be studded with tumor nodules. The lymph-nodes usually show secondary growths. It is said that the liver is less apt to be the seat of the secondaries than the lungs.

The large spindle cell tumors, when carefully studied, frequently turn out to be of muscular derivation, and perhaps should be described as malignant myomas, or myo-sarcomas. They are supposed to originate in the occasional small knots of muscle tissue found in the wall of the stomach, or from the *myomas* well known as small, sessile or sometimes polypoid tumors of its outer wall.

More rare are the *lipoma* and *fibroma*. They are situated between the coats, are usually quite small, and harmless.

Angioma of the stomach seems to be very rare. Lemon, of the Mayo Clinic found 5 in the literature, and added another, a total of 6 reported cases.

Adenoma of the stomach may occur, but the reported cases are not convincing. Some of them upon careful investigation prove to be fragments of pancreatic tissue included in the gastric wall—such was the case with one that I reported many years ago—or else to be polypi or papillomatous growths from the mucosa.

Foreign Bodies in the Stomach

Most foreign bodies capable of entering the stomach are also capable of leaving it, unless of a very irregular shape, or provided with sharp points that fix them in position. Moreover, most of them enter with the knowledge of the patient who, except in cases of insanity, is able to explain their presence. Confirmation of alledged swallowing of false teeth and other objects is now easily achieved by fluoroscopic or X-ray examination, and the presence or absence of the body, or its progress through the alimentary tract having been determined it usually becomes an easy matter to decide upon the appropriate treatment. One exception to this, however, rare in human beings, is the hair-ball or aegagraphilus. About 50 cases are reported, nearly all in young women of nervous temperament, who bite off and swallow the ends of their plaits or braids. In the course of time the long hairs collect and are rolled into a ball that can no longer pass the pylorus, but collects insoluble food remnants in its meshes, and becoming coated and saturated with mucus, may undergo partial calcification. On account of their J-shape, hair balls are usually readily diagnosticated by Roentgenogram.

37

THE DUODENUM

The duodenum, that portion of the small intestine that begins at the pyloris and extends some 30 centimeters to the upper part of the second lumbar vertebra, forms a complicated sigmoid loop, the descent and ascent of which almost complete a circle, and embrace the spinal column and head of the pancreas.

FIG. 382.—Posterior view of a hair-ball tumor removed from the stomach of a little girl of 10 years: gross specimen. (*Carroll.*)

The upper part of the inner surface, for a short distance, is fairly smooth, and the mucosa is thickly beset with the glands of Brunner. As it is descended, they become less numerous and more scattered, and irregular transverse folds make their appearance. Upon the inner and posterior wall, at about the junction of the upper and middle thirds, and about 10 cm. from the pyloris, usually hidden by one of the folds of the mucosa, there is a little eminence with a central opening into which a probe can easily be introduced in spite of a tiny sphincter

muscle with which it is provided.   It is the *papilla of Vater*, and the outlet of
the common bile duct and the major pancreatic duct, that of Wirsung.   If the
point of a pair of scissors be introduced and the orifice enlarged, it will be found
to open into a small bulbous space, the *ampulla* of Vater, into which both the
ductus communis choledochus and the duct of Wirsung empty.   The probe
introduced as suggested, may find its way into either of these according to the
position of a membranous flap just inside the opening.   But if the probe first
enter the bile duct, it may be difficult thereafter to introduce it into the
pancreatic duct, and vice versa.

Below this point the transverse folds become more and more distinct until
they become the well known valvulae coniventes of the jejunum.

Above the papilla of Vater the duodenum receives the acid contents of the
stomach, and it is there, as has already been pointed out, that peptic ulcers of
the duodenum occur.   Below it the admixture of the alkaline pancreatic juice
and bile destroy the acidity, and no peptic ulcers occur.

The posterior wall of the upper third of the duodenum is occasionally the
seat of a small diverticulum, usually just large enough to admit the tip of the
fore finger, and about as deep as half the length of the first joint.

In the absence of any better theory of origin, such diverticula are supposed
to be formed through the distension of a weak part of the wall of the organ.
They may mark points of yielding prior to the healing of peptic ulcers.

The duodenum is remarkably free from diseases of its own, but the relation
of its upper end with the most frequently diseased portion of the stomach, its
intimate relation to the pancreas, and the passage of the important ducts
of the liver and pancreas through its wall to open into its interior, cause it to
participate in numerous of the troubles of its neighbors.

The opening made into the ampulla of Vater, if continued upward and to the
right, lays open the common bile duct which will be found to be about 7 cm. in
length, from its ending in the ampulla below to its beginning at the orifice of the
cystic duct above.   It varies considerable in diameter, measuring about 6–7 mm.
—a little smaller than a common lead pencil.   It is continuous, without change
of diameter, with the hepatic duct, which continues almost to the hilum of the
liver, where it divides into two main branches, one for each principal lobe of
the organ—a distance of 2–4 cm.

The cystic duct opens into the right side of the common duct, going off at an
acute angle for a distance of 3–4 cm. through the gastro-hepatic omentum, and
a fold of peritoneum, to the gall bladder.   It is difficult to open because of its
somewhat spiral or angulated course, and because of certain folds of mucous
membrane scattered along its length like transverse valves.

The gall bladder, a pyriform saccular structure occupying the fissure of the
gall-bladder on the under surface of the liver, is variously looked upon as an
organ, and as a diverticulum of the bile ducts.   The bile ducts consist of a
mucosa covered with columnar epithelial cells, beneath which is a fibro-elastic
layer containing numerous unstriated muscle cells.   The muscle becomes thicker
as the cystic duct is ascended, and develops into a special muscular coat of the
gall-bladder.   The gall bladder itself is lined with a mucous membrane the

greater part of which is both villous and rugose, and covered with columnar epithelium. In some cases deep gland-like crypts occur at the bottom of the folds—*Luschka's pockets* or *crypts.* Beneath the mucosa is a fibro-elastic vascular sub-mucosa, and beneath it the muscularis. Outside of these, and derived from the peritoneal investiture, are a subserous and serous coat. The

FIG. 383.—Microscopic section of the wall of an inflamed gall-bladder, showing Luschka's glands. The inner surface with imperfectly preserved columnar epithelial lining and enormously swollen villi s seen below, the Luschka's glands above. (*From a specimen in the Lankenau Hospital of Philadelphia.*)

gall bladder is about 8 10 cm. in length, and has a capacity of about 50 cc. Its greater extremity is opposite the cystic duct, and forms a blunt rounded caecum that reaches to the margin of the liver anteriorly.

The physiology of the gall bladder is still controversial. It seems to be chiefly intended to relieve the more delicate bile ducts from accidental internal pressure, yet when the gall bladder is experimentally removed, or is destroyed by disease, the ducts seem to suffer no ill effects in consequence. It certainly performs the function of abstracing water from the bile, though how much reaches it for that purpose, and what advantage such inspissation may be are unknown.

Rich plexuses of lymphatics course between the coats of the gall-bladder, connecting with nodes situated in the transverse fissure of the liver and along the

duct in the gastro-hepatic omentum, these in turn communicating with others—
the diaphragmatic nodes—situated about the vena cava.

The tissues of the cystic duct and gall-bladder are supplied with blood
by the cystic branch of the hepatic artery, which terminates in capillaries that
not only ramify in the submucosa, but also send minute branches into the villi
of the mucosa almost to their tips.

If from the ampulla of Vater the scissors be directed into the pancreatic
duct of Wirsung, it will be found to ascend slightly through the head of the organ,
then turn directly toward the left, continuing to its tail. Its length is therefore
between 12 and 15 cm., and its greatest diameter not more than 5 mm. As soon
as it is opened one is struck by the pearly white color of its inner surface as con-
trasted with the yellow color of the bile ducts. If any part of the pancreatic
duct system should show yellow color, it is to be interpreted as biliary staining,
and looked upon as abnormal. These larger pancreatic ducts are composed of
thick fibrous walls, in which there seem to be occasional unstriated muscle
cells.

But the duct of Wirsung is not the only pancreatic duct. The head of the
organ, embryologically its oldest part, discharges its secretion through the
duct of Santorini, originally the chief duct, but in adult individuals greatly
modified, and usually superceded by that of Wirsung. It will be remembered
that the pancreas originates from three diverticulations from the duodenum.
The dorsal rudiment grows most rapidly, and becomes separated from the
. others through the general growth of the alimentary canal, so that it soon
appears considerably above them, its duct, that of Santorini entering the duode-
num entirely alone. The ventral rudiments, consisting of a right and left, arise
in connection with the primitive bile ducts, in such manner as to make it doubt-
fully correct to say that they are really diverticulations of the duodenum itself
rather than of the bile duct. The left rudiment soon becomes extinguished and
disappears, but the right grows slowly, being displaced toward the left, meeting
the dorsal rudiment and fusing with it. The duct of this ventral portion which
later forms part of the body of the organ and all of its tail, discharges its secre-
tion through the duct of Wirsung.

However, as the two portions grow, the ducts anastomose, after which it seems
to be a matter of chance which of them shall preponderate, and just how the
secretion shall be discharged.

In the greater number of cases the duct of Wirsung becomes the chief duct
and in many the duct of Santorini becomes small and comparatively unimportant,
or through the anastomosis with it becomes but a tributary. In a few cases the
reverse is true and the duct of Santorini remains the chief duct. In a few cases
the duct of Santorini ceases to open into the intestine at all.

Opie tabulates the condition of the ducts as he found them in specially
prepared and carefully studied specimens as follows:

I. Ducts in Anastomosis.
   1. Duct of Wirsung larger.
      (*a*) Duct of Santorini patent.. 63
      (*b*) Duct of Santorini not patent.. 21

2. Duct of Santorini larger or equal in size to that of Wirsung.

    (a) Duct of Wirsung patent.......:.. 6

    (b) Duct of Wirsung not patent.. 0

II. Ducts not in anastomosis.

    1. Duct of Wirsung larger.. 5

    2. Duct of Santorini larger.. 5

When present, the duct of Santorini opens through an orifice in a usually well concealed tiny papilla upon the posterior inner wall of the duodenum about 3 cm. above and a little to the inner side of the papilla of Vater.

The relation of biliary and pancreatic ducts in the papilla of Vater is also subject to variation that has some pathological importance. The relation is thus brought out by extracts from the work of Opie:
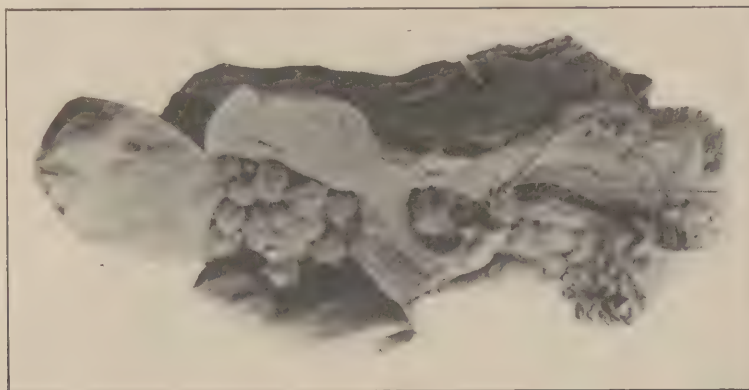
Fig. 384.—A gall-bladder showing cholecystitis and cholelithiasis, with a stone (a) impacted in the cystic duct. (*From a specimen in the Pathological Museum of the University of Pennsylvania.*)

"The common bile-duct descends toward the duodenum alongside the head of the pancreas occasionally imbedded in its substance and comes in contact with the duct of Wirsung, beside which it lies for a short but variable distance before entering the wall of the intestine. . . . In fifteen cases (37.5%) the duct lay in a groove upon the surface of the gland often converted into a canal by the adjacent duodenum. In the remaining twenty-five cases (62.5%) the duct was completely surrounded for a variable distance by pancreatic tissue. . . . The ductus choledochus and the duct of Wirsung penetrate side by side the coats of the duodenum, through which they pass obliquely a distance of about two centimetres and cause a papilla-like elevation of the mucous membrane. Within the papilla they unite to form a short common cavity — the diverticulum of Vater. At the point where the common duct enters the wall of the intestine it is constricted, or at least but little distensible, so that gall-stones often lodge in this situation.

The description of the diverticulum or ampulla of Vater, given by different anatomists does not vary materially. It may be described as a conical cavity into the base of which open two ducts; the apex situated at the summit of the diverticulum, is their common duodenal orifice. According to Testut, its length varies from six to seven millimetres, according to Sappey, from seven to eight millimetres. Occasionally the two ducts have no common channel, but open by separate orifices upon the summit of the bile papilla. Claude Bernard describes a mode of termination which has since been observed by others. The bile duct is prolonged as far as the mucosa of the duodenum, upon which it opens by a circular orifice. The terminal part of the pancreatic duct, like a gutter, embraces the bile duct, and its orifice has the outline of a crescent."

The orifice of the diverticulm of Vater constitutes the narrowest part of the bile-channel, and here small calculi not infrequently become impacted."

Piersol says of the lymphatics of the pancreas:

"They take origin from a perilobular network from which collecting stems pass to the neighboring nodes following the course of the blood-vessels which supply the gland. The great majority of them pass to the chain of splenic nodes which extends along the upper border of the pancreas, but those of the head of the gland pass in part to nodes of the hepatic group, following the course of the superior pancreatico-duodenal vessels, while others again accompany the inferior pancreatico-duodenal vessels to terminate in nodes belonging to the mesenteric group."

The orifice of the ampulla of Vater is guarded by a sphincter muscle, so adjusted as to open and permit the outflow of bile and pancreatic juice during the period of digestion, and to close to prevent regurgitation between them. In this manner frequent infection of the liver, gall-bladder and pancreas is prevented.

However, infections of all of these parts occur, and it becomes interesting to investigate through what routes. It may at once occur to the reader that if intestinal contents should gain admission to the ampulla of Vater, the contained infectious agents might be transmitted to all or any of the ramifications of the biliary and pancreatic structures and well as to the gall-bladder, and the possibility is undeniable. But to do so, they would have continuously to travel against the natural currents except in the case of the gall-bladder which is supposed to fill by regurgitation from the over-distended common or hepatic ducts. It would seem then that except in cases of disease interfering with the action of the sphincter, infection by this route should be pretty well guarded against. A second possibility presents itself in cases of inflammatory disease of the duodenum in which the infectious agents admitted to the lymphatics, might reach the gall-bladder or pancreas through those vessels. To do so, however, the natural currents would have to be reversed. The remaining possibility is that of infection from agents brought to the liver, gall-bladder or pancreas through the circulating blood, as is known to occur in many infectious diseases, and therefore offers the best explanation of the common source of infection. But the other possibilities, especially the regurgitation of bile into the pancreatic duct must be borne in mind.

Should the infection localize chiefly in the bile ducts, the swelling of the lining membrane, trivial in other parts of their course, may close the diminutive orifice of the papilla of Vater, with the double effect that neither the bile nor the pancreatic juice could enter the intestine, and that the bile, of which the quantity preponderates, might flow in increased quantity into the gall-bladder, or, as is much more dangerous, into the pancreas.

Under these circumstances, conceiving the gall-bladder to be especially devised for relieving the occasional excessive pressure in the bile ducts, it might be inferred that the gall-bladder would greatly dilate. But this it rarely does. The biliary obstruction spends itself chiefly upon the bile ducts, which dilate. The secretion, unable to escape, backs into the finer radicles some of which yield to the pressure, rupture, and permit the bile to enter the lymphatics and so reach the blood where its presence is shown by jaundice. If attacks of *catarrhal*

cholangitis be repeated several times, a chronic disturbance may develop in which the stagnation of the bile predisposes to the appearance of a new factor—the gall-stone.

Gall-stones are biliary calculi formed most frequently in the gall-bladder, next most frequently in the common bile duct, and less frequently in other parts of the biliary duct system. Stagnation of the bile undoubtedly predisposes to them, and they are composed of the various precipitable substances contained in the bile in health and disease.

The gall-bladder because of its muscular coat, is capable of emptying itself more or less completely, but how frequently it does so, and under what circum-
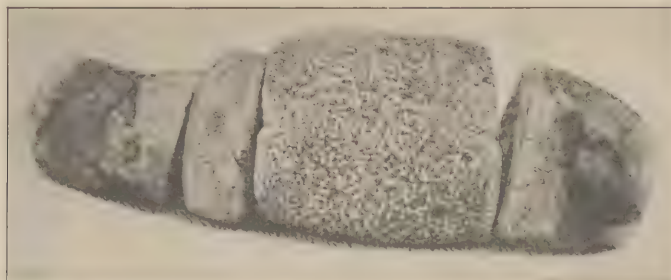
Fig. 385.—Mass of gall-stones (natural size) removed from the gall-bladder of an old woman. In this case there was no history of hepatic disorder.

stances is not known. If its chief function be the inspissation of the bile, it is presumably commonly present in inspissated form, and experience shows that at times its contents are very thick and viscid. But when to such conditions as are known to be normally present there are added the disturbances incidental to inflammation, the predisposition to the formation of the calculi is greatly increased. It is well known that the respective micro-organisms of typhoid fever, influenza, and other bacteraemias frequently invade the gall-bladder with destructive catarrhal, purulent, ulcerative, and even gangrenous lesions, but with these we will not concern ourselves, and it is not within the scope of this work to discuss the infectious diseases except as they have especial significance in the explanation of less easily understood conditions. It is not now the infectious disturbance itself so much as the changes to which it later leads that interest us.

Recovery from interstitial inflammation finds the wall of the gall-bladder thickened, or thinned, as the case may be, but in either diminished in contractile power, so that the stagnation of the bile is increased. The catarrhal inflammation adds to its contents more or less of the products of inflammation, both predisposing to the precipitation of the solids and the formation of calculi. *Cholelithiasis*, or *gall-stone disease* is therefore the common sequel of infection of the gall-bladder, even though it may still be difficult or impossible to describe exactly how the stones are formed.

Presumably, the clumps of bacteria, the flakes of mucus, the groups of desquamated epithelial cells, or other additions to the contents form the nuclei about which the pigments and salts of the bile are precipitated in varying propor-

tions in different cases according to the composition of the bile in the gall-bladder at the time, and to the chemical conditions of their precipitation. Experience shows that most of the stones are chiefly composed of bilirubinate of calcium infiltrated with cholesterin; more rare calculi are composed entirely of cholesterin, and still more rare ones of calcium carbonate. A large and dis-

Fig. 386. —Impaction of a gall-stone in the ampulla of Vater, closing the opening of the papilla duodeni (⅔ natural size). *a*, Duodenal mucosa; *b*, calculus projecting from the papilla; *c*, greatly dilated ductus communis choledochus; *d*, opening of the cystic duct. (*Johres.*)

tended gall-bladder sometimes contains only a single small calculus; a small and contracted one may be filled with large and small calculi. The presence of a calculus immediately sets in motion the mechanism required for the formation of others. A calculus is a cause of additional cholecystitis, and as has been seen, cholecystitis is the most frequent cause of gall-stones. The more stones the patient has, and the longer he has them, the greater the probability that he will have still more, or that those he already has will grow larger.

Supposing a stone to have formed, the cystic duct being patulous, there is a tendency for it to pass into the duct, and if less than about a centimetre in diameter, to descend to the common duct. The passage of the stone through the cystic duct must depend upon the muscular contractions of the gall-bladder and the pressure of the bile behind it. Whether this results in pain is difficult

to determine, it probably does. But if the stone reaches the common duct, the small size of the orifice of the ampulla of Vater makes further passage difficult, and for a time, at least, it comes to rest, with the result that the common duct is obstructed. This obstruction may be followed by severe jaundice, and great pain may result from the distension of the hepatic ducts by the retained bile under abnormal pressure. But under these circumstances the gall-bladder does not dilate as might be expected. At least it does not do so in more than 80% of the cases, and its failure to do so has been formulated into what is now commonly spoken of as *Courvoisier's law*, Terrier's law, or the Courvoisier-Terrier law. This is, that when the common bile duct is obstructed by a gall-stone, the gall-bladder does not dilate, though when the common duct is obstructed from other causes it commonly does. This is not so difficult to understand as might at first seem. There is first of all the morbid condition of the gall-bladder (cholecystitis with cholelithiasis) itself, that makes dilatation difficult, second the not infrequent simultaneous obstruction of the cystic duct by other stones on their way to the common duct, which the bile cannot pass, and third, the obstruction afforded by the stone at the papila of Vater is probably but rarely so complete as to prevent any bile from passing. It more commonly acts as a ball valve, permitting bile to pass intermittently.

The stone in the ampulla of Vater may eventually effect sufficient dilatation to permit it to escape, when the patient recovers from the attack of biliary colic and remains well until another stone descends. Experience shows that once a patient has a gall-stone, he is liable to others, and that even if he does not suffer further attacks of biliary colic because the cystic duct closes, it is probable that new stones will form in his gall-bladder. If as the result of inflammation, or the impaction of a stone, the cystic duct become closed, and no more bile can enter, contrary to what might be expected, the gall-bladder may enlarge. Its ability to do so, however, must depend partly upon the condition of its wall. If it be much modified and thickened by the antecedent inflammatory disturbance, it may do the reverse and shrink. Any enlargement however, must depend upon the collection of some fluid other than bile, and is to be attributed to exudations and secretions. For a long time the appearance may be that of bile because sufficient bile is still present to color the fluid, but as time passes, the pigments are precipitated or absorbed, and the fluid losing its color ceases any longer to be bile, but becomes exudate. Distended gall-bladders filled with cloudy fluid are not uncommon, filled with clear watery fluid, *hydrops vessicae felleae*, they are rare.

But in most cases with gall-stones, the bladder either remains of about normal size, or shrinks. There are exceptions, of course, as in those cases where a gall-bladder harbors an enormous stone, or in which it contains an enormous number of stones.

There seem to be some cases in which biliary calculi remain almost indefinitely in the gall-bladder without doing noticeable damage. But in most cases the opposite is true. The traumatic injury effected by the stone not only seems to facilitate the continuous activity of such micro-organisms as may already be in the interior or wall of the gall-bladder, but also favors the successful coloniza-

tion, of such others as may be brought there by the blood. The result is continued inflammation, with occasional suppuration, the occurrence of fever of irregularly intermittent type—*Charcot's intermittent*—and additional gall-stone formation.

Acute infection, whether purulent or necrotic, sometimes results in perforation of the gall-bladder, and the purulent and necrotic complications of cholelithiasis make the accident more frequent where gall-stones are present. Uncomplicated cholelithiasis, however, rarely if ever results in perforation, probably because the presence of the stone in the bladder is followed by more or less thickening of the wall of the viscus, thus strengthening its tissue so as to enable it to resist the pressure of the stones. In case of perforation associated with gall-stones, the contents of the bladder rarely escape into the abdominal cavity, because adhesions usually form in advance of the accident, and localize the damage. Should peritoneal escape occur, fatal peritonitis may be expected unless prompt surgical intervension can be practiced. This is not on account of the escape of the bile, but of the distribution of the infective micro-organisms that it is sure to contain. In perforation with localized escape of the contents of the gall-bladder, purulent pericholecystitis is the rule. The abscess at first localized, soon proceeds to burrow, and finds numerous outlets with the formation of fistulas. These may be external, the purulent contents of the abscess and gall-bladder escaping externally, or they may be internal, and the fistulas then communicate with various viscera as is shown by Courvoisier in his study of 499 cases:

Perforation externally	196
Perforation of the duodenum	83
Perforation of the peritoneal cavity	70
Perforation of the peritoneal pouches	49
Perforation of the colon	39
Perforation of the pleura and lung	24
Perforation of the stomach	13
Perforation of the bile-duct-system	8
Perforation of the urinary tract	7
Perforation of the portal vein	5
Perforation of the retro-peritoneal tissues	3
Perforation of the jejunum	1
Perforation of the ileum	1
	499

In some cases the perforation, with the escape of the contents including the calculi, may be followed by healing, but in such cases, as in those in which the surgeon operates and removes the stones, the gall-bladder remains diseased, and new stones are likely to form subsequently, so that the disturbance cannot be said to be self limiting. Of course the removal of the gall-bladder effects a final cure.

In cases in which the gall-stone passes into the common duct, it does not always escape through the opening in the papilla of Vater, but may remain either in the ampulla or higher up in the common duct.

There it increases in size as time passes, and there it is frequently joined by other calculi later descending the duct. Many calculi may thus collect, dilating the ducts to an enormous size. Deaver has reported the case of a woman
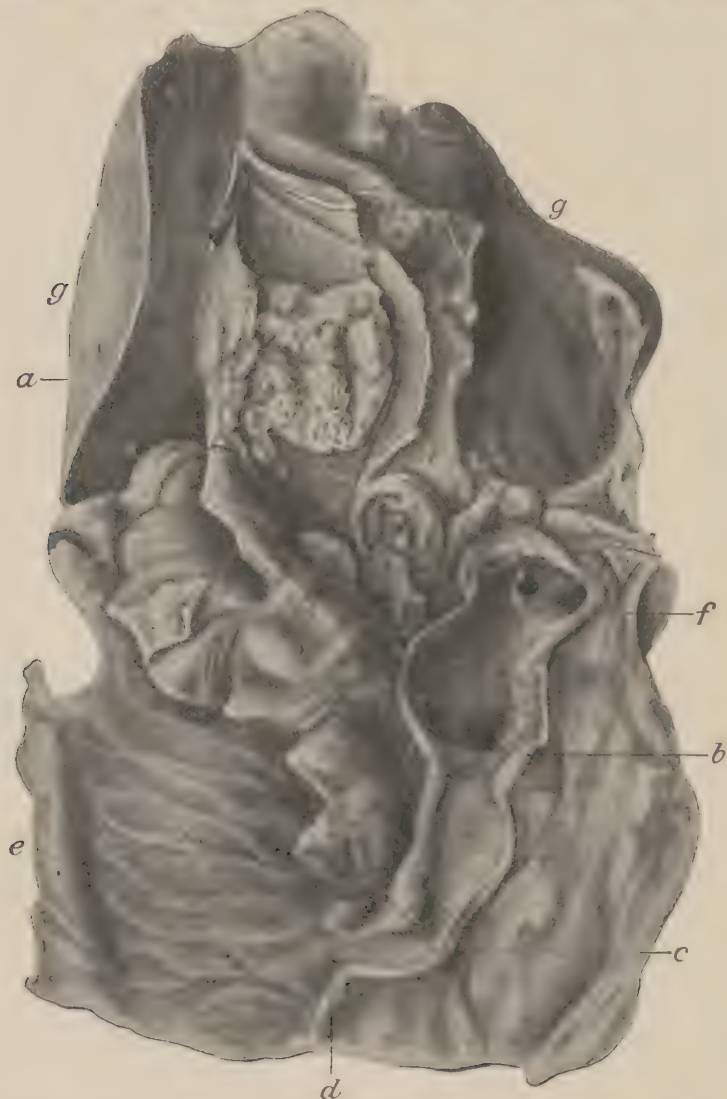
Fig. 387.—Carcinoma of the gall-bladder with a stenosing metastasis in the ductus communis choledochus (⅔ natural size). *a*, Carcinoma of the gall-bladder; *b*, upper, and *c*, lower border of the carcinomatous infiltration of the common bile-duct; *d*, duodenal opening of the common duct; *e*, duodenal mucosa; *f*, division of the hepatic duct into branches. (*Johres.*)

aged 34 years, who suffered for nine years with indigestion and epigastric pain, from whose gall-bladder he removed 55 stones, and from whose ducts he removed 258 other stones varying in size from a millet seed to a large pea.

Stones in the duct bring about stagnation of bile, cholangitis, and thus predispose to the local increase in the size of the stones harbored, as well as

tending to new formation of stones in the duct itself, as is shown by their presence in the hepatic duct, and sometimes its larger branches.

Carcinoma of both the gall-bladder and bile ducts scarcely occurs without the presence of gall-stones. It has long been a mooted question whether the carcinoma was the primary disturbance, the formation of the stone being the result of the stagnation of the bile incidental to the obstructions and other morbid conditions resulting, or whether the gall-stone was primary, the carcinoma resulting from the irritation it excited. The question cannot be answered in the present uncertain state of knowledge of carcinoma, but the greater number of authorities believe that the cancer is the result of the irritation effected by the stone. This view is quite consistent with the generally accepted view that where a carcinoma primordium exists, irritation may cause its development. The great number of cases of gall-stones in which no carcinoma results may be explained by the supposition that in them no primordium of cancer development existed.

Carcinoma of the gall-bladder is rarely a large tumor, and commonly results in shrinkage and dense connective-tissue formation so as to resemble scirrhus. In rare cases it may be gelatinous, then attaining to a larger size. Microscopically it assumes a variety of appearances. It is most commonly a cylindrical cell tumor, but carcinoma rotundocellulare is not uncommon, and squamous cell carcinoma with epithelial pearls is known to occur.

Carcinoma of the bile-ducts is most frequent in the neighborhood of the ampulla of Vater. It almost always forms a dense scirrhus tumor whose microscopic structure is carcinoma rotundocellulare. Carcinoma of both the gall-bladder and the bile-ducts is apt to remain small, though prompt to give metastasis to the liver. Local extension of the tumor of the bile-ducts to the head of the pancreas, directly below, is almost invariable and complicates the surgical treatment.

THE PANCREAS

Inflammatory disturbance of the pancreatic duct system, initiated through irritants entering from the circulation blood, or from the bile duct or intestine, may result in the formation of calculi—*pancreatic sialolith*—or concrements. They are of a whitish, yellowish or grayish color, sometimes smooth, sometimes porous upon the surface, and occasionally branched in correspondence with the duct system in which they occur. Their size varies from a pin head to a pigeon-egg.

Whether such stones frequently escape into the intestinal contents is a question, as knowledge of them is almost entirely confined to those found in the pancreatic ducts themselves. Should any find their way into the ampulla of Vater and there remain, they would soon become so incrusted with the bile pigments and salts as no longer to be recognizable as having originated in the pancreas.

The stones are formed through the deposit of calcium and magnesium carbonate in an organic matrix supposed to be inspissated secretion and inflammatory exudate.

Pancreatic calculi seem, at times, to exist without doing much damage, being found unexpectedly at autopsy. They may, however, excite inflammation, and if infection occur, may lead to suppuration, and even perforation of the ducts. The stones are composed of material opaque to X-rays, throw good shadows, and so may be discovered during life.

The obstruction of the pancreatic ducts by a calculus may result in *chronic interstitial pancreatitis*.

Fig. 388.—Acute hemorrhagic necrosis of pancreas: cholelithiasis and impaction of a small gall-stone in the common duct and in the ampulla of Vater. Abundant fat necrosis. (*MacCallum.*)

Infectious agents reaching the pancreas through the blood, the lymphatics, or perhaps sometimes through the ducts from the ampulla, may also excite *acute purulent pancreatitis*, characterized by abscesses of varying size. These usually develop slowly but may rapidly attain to considerable size. They may resorb, but more frequently rupture into the stomach, duodenum or peritoneal cavity. Pylephlebitis with abscess of the liver sometimes follows as a complication, and the greater number of cases terminate fatally.

Acute hemorrhagic pancreatitis is characterized by the occurrence of more or less extensive areas of necrosis alternating with more or less extensive areas of hemorrhagic extravasation into the tissue of the pancreas, which sometimes becomes gangrenous. Fortunately it is rare, as it develops with great rapidity and may prove fatal in a few hours and seldom recovers. Its occurrence is mysterious and not all cases have been satisfactorily explained. It seems, however, as though the greater number of cases may be referred to the entrance of bile into the pancreatic ducts as the result of the obstruction of the ampulla of Vater by a gall-stone.
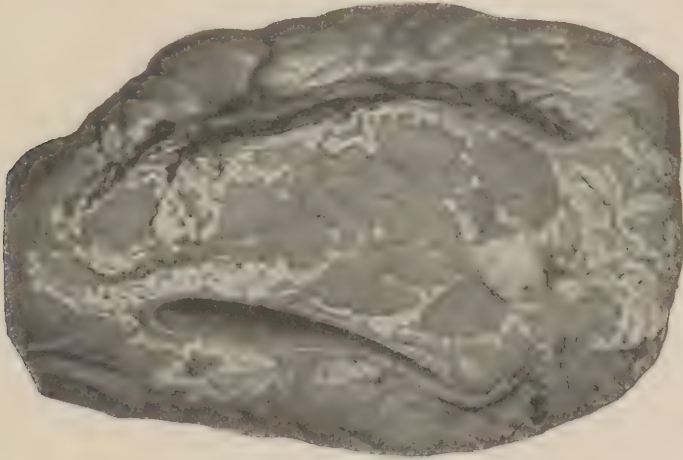
FIG. 389.—Fat necrosis of the pancreas. (*Aschoff.*)

This theory of origin is supported both by experimental and pathological evidence. Thus, Thiroloix by injecting deliquescent chloride of zinc; Hlava, by injecting artificial gastric juice; Carnot by injecting a solution of papaine; Flexner by injecting a variety of chemical irritants, and Opie by injecting bile into the pancreatic ducts of dogs, in nearly all cases produced lesions closely resembling those of hemorrhagic pancreatitis. On the clinical side is the observation that in the greater number of cases, acute hemorrhagic pancreatitis is associated with cholelithiasis.

But it seems certain that gall-stones do not occur in all cases, therefore cannot be the only etiological factor.

The introduction of the various mentioned chemical substances, or of bile into the pancreatic ducts effects more or less wide-spread injury and probably exposes the pancreatic issue to the digestive influence of its own tryptic enzyme, thus causing the further destruction of tissue, and erosion of blood-vessels. There is nothing specific in the nature of the injury effected, and any other damage to the pancreatic tissue, might result in the same condition. Indeed clinical acute hemorrhagic pancreatitis has been observed to follow traumatic injury, and a few cases have seemed to follow hematogenic intoxication.

The interesting question is why necrosis and hemorrhage of an organ not immediately indispensible to life should give rise to such intense and rapidly

fatal symptoms. Some refer it to the close relation that the tissues of the pancreas bear to the solar plexus of the sympathetic nervous system, others ignoring this altogether, refer it to intoxication from the absorption of the split protein substances resulting from the digestive effect of the pancreatic juices upon its necrotic tissue. Each of these may have its moiety of truth, but the latter is particularly supported by the now well known phenomenon of acute pancreatic intoxication in dogs. If into the carefully and aseptically opened abdominal cavity of a dog a sterile fragment of pancreatic tissue be introduced, although the wound heal kindly and the dog recover from the operation, death almost invariably follows the disintegration and absorption of the introduced tissue.

In any disease or injury of the pancreas followed by the escape of its secretion into its own tissue, or into adjacent or even remote regions, a peculiar and interesting, though not in itself important or dangerous phenomenon is observed to occur in the adipose tissue. It is transformation by the lipolytic ferment steapsin, and is known as "*fat necrosis.*" It may be observed in the course of a few hours, and is characterized by the disappearance of the yellow color normal to the human fats, and its replacement by a substance of whitish color and a firmer and putty-like consistence, which later becomes crumbly, and eventually may calcify. It signifies to the surgeon that pancreatic juice has escaped its normal bounds, thus indicating some destructive disturbance of the organ.

Carcinoma of the pancreas is not uncommon. Bashford found 526 cases among 33,788 cases of carcinomas in males, and 474 cases among 50,660 carcinomas in females. Any part or all of the pancreas may be effected, but the most frequent localization is the head of the organ. In many cases the primary tumor is very small, though its early metastasis to the liver results in extensive disease of that viscus, so that occasional cases are regarded as primary carcinoma of the liver that are, in reality, secondary. The tumors are most frequently distinctly scirrhus, and as obstruction of the pancreatic ducts soon follows, with secondary chronic interstitial pancreatitis, far greater areas of the pancreatic tissue appear to be diseased than are really the seat of carcinoma. In a few cases the disease tends to spread widely, involve the greater part of the head of the organ, and infiltrate the suprajacent duodenum, beginning about the bile ducts. It may then be difficult if not impossible to determine where the carcinomatous disease really began. In rare cases the carcinoma of the pancreas is soft and massive, and in a very few cases it is gelatinous. As, however, gelatinous carcinoma of the pylorus is frequent, care must be taken to exclude the possibility of disease chiefly situated in the pancreas having begun in the pyloris.

The histology of the lesion varies. In many cases it is a cylindrical-cell adeno-carcinoma; in others a cuboidal-cell carcinoma. This has lead to differences of opinion concerning its probable origin, some believing that it arises from the ducts, others from the alveolar tissue of the organ. The tendency to early massive metastasis to the liver, the invasion of the duodenum with closure of the bile ducts, the associated chronic interstitial pancreatitis with loss of pancreatic juice, all tend to make the disease rapidly fatal. Patients rarely live more than

a year after symptoms can be recognized. Metastasis to the bones is sometimes a distressing complication. Surgical intervention in the very early stages of the disease, and before the duodenum and bile ducts are involved,
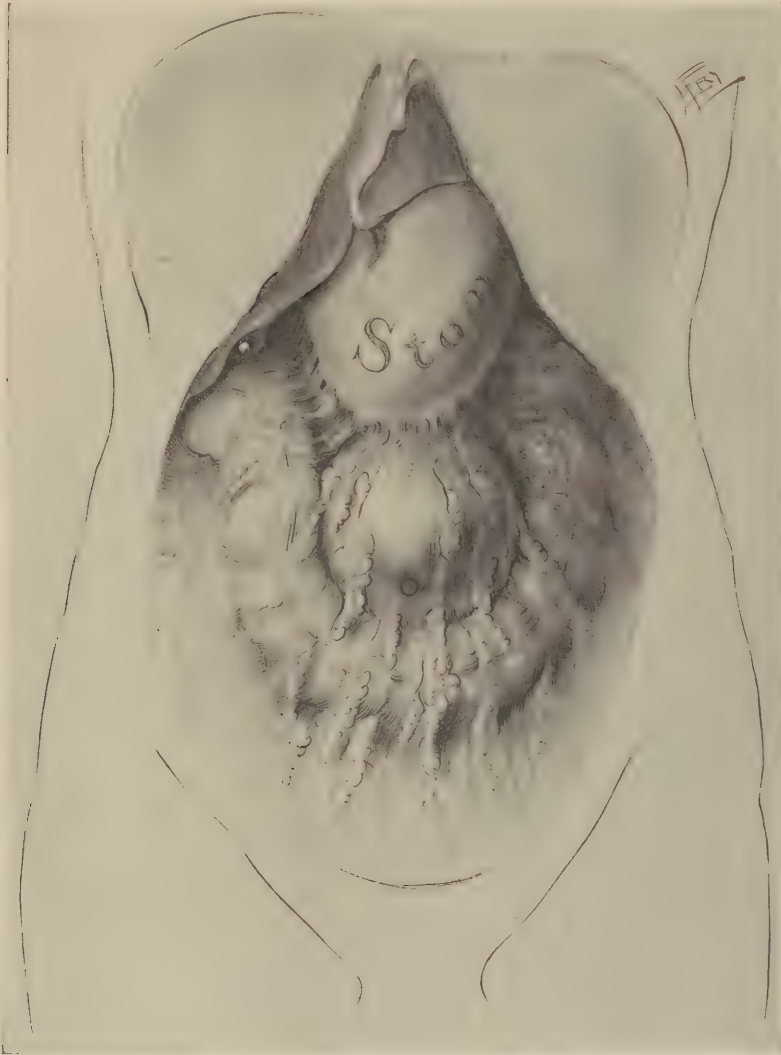
FIG. 390.—Pancreatic cyst between the liver and the stomach, covered anteriorly by the gastrohepatic omentum. (*Judd.*)

greatly mitigates the condition of the patient, but offers little hope of recovery on account of the early metastases to the liver which cannot be discovered, or if found cannot be removed. It also lessens the frequency of the distressing jaundice with its accompanying intense itching, and makes the patient much more comfortable, as well as prolonging his life somewhat.

Cysts of the Pancreas.—These are relatively rare lesions that make their appearance in one or the other of two quite different forms.

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First, the clinically unimportant small cysts that are either congenital or may result from obstruction of the small ducts, and appear as single or multiple rounded pea-sized or cherry-sized spaces in and upon the pancreas, filled with accumulated and more or less altered secretion. These are accidentally encountered at operation or at autopsy. It is not always possible to recognize the congenital lesions, as such, but the association of multiple cysts of the pancreas with multiple cysts of the liver and kidneys is supposed to be significant of a general congenital cystic disturbance.

Second, the clinically important large cysts.—These occasion symptoms according to their size, and the mode and rapidity of their formation. They can be diagnosed during life, and of Judd's cases only three were discovered accidentally during operation for other causes. Körte collected from the literature 121 cases that had been operated upon, and Judd recently analyzed 41 cases observed in the Mayo Clinic, of which 38 were operated upon.

The cysts occur at any age from infancy to senility, and attain to any size, the largest recorded having filled both abdomen and pelvis. They are usually of a pint or quart capacity, and being fluctuating and more or less movable, may be diagnosed when physical findings, clinical history, symptoms and X-ray or fluoroscopic findings are combined. They may be removed, though the operation cannot be said to be entirely free of danger, and they do not recur. In two of the cases in Judd's collection there was associated malignant disease. Ruling these, as well as one dermoid that contained hair and one tooth, and one hemorrhagic cyst out of the present consideration, it is found that there are true cysts and pseudo-cysts.

The former are filled with light-colored viscid fluid containing mucin, and pancreatic enzymes. In 54 cases whose contents were studied for the demonstration of enzymes, one ferment was found in 20, two ferments in 20, and all three ferments in 14.

The pseudo-cysts may also contain clear and light-colored fluid, but are apt to have darker and more hemorrhagic contents. As some of the cysts are very old when they come under observation—one is said to have had a known existence of 47 years—there is great likelihood of substantial change in the contents. It has been asserted that in a few cases bile has been found in pancreatic cysts, but Judd thinks that in those cases not enough care may have been exercised to make sure that the cyst did not connect with the bile duct.

Körte found his 121 collected cases to embrace 60 men, 50 women and 5 in the sex was not mentioned. Judd's 41 cases were divided into 24 women and 17 men.

The etiology of the large cysts is very obscure. Of Körte's 121 cases it was possible to make three groups:

1. Those with a history of traumatism, of which there were 33, 30 being men.
2. Those with a history of inflammatory disease of which there were 51.
3. Those without any explanation, of which there were 33, 26 being women.

The traumatic cases may result from injury followed by interstitial hemorrhage and colliquation of the injured and hemorrhagic tissue, resulting in pseudo-cysts with hemorrhagic or dark colored contents, growing paler as time goes on.

The cases with inflammatory symptoms such as repeated attacks of pain resembling biliary colic, may suffer from obstruction of branches of the ducts, and collection of secretion supplemented by inflammatory exudates.

The unexplained cases—those with no suggestive history—may be in part referred to the occurrence of some such cystic disturbance as has been called cyst-adenoma. A few may result from plugging of the ducts. One must, however, be careful in regard to accepting the last suggestions, as cysts of the pancreas cannot be experimentally produced by ligation of the ducts.

Hydatid or echinococcus cysts are, or course, not included in this discussion.

THE VERMIFORM APPENDIX

The vermiform appendix, found only in man, certain anthropoid apes and the wombat, is the undeveloped rudiment of the large caecum found in many of the lower animals, just as the caecum of those animals is but the rudiment of the enormous caecum found in herbivorous animals and rodents, as is pointed out by Piersol. Physiologists have found no function for it, and it probably has none of its own, and shares so small a part in the general activity of the intestines as to be neglegible in importance. Experience certainly shows that its removal is not incompatible with perfect subsequent health, and as it frequently becomes diseased in such manner as to cause suffering and in not a few cases death, it is generally conceded that it is better to be without it, lest it cause future trouble. With this view of possible future evil in mind, it is now recommended that in all cases, the appendix be removed whenever the abdominal cavity is opened, no matter what the original purpose of the operation. Normal appendices are therefore removed every day as a part of surgical routine.

When, therefore, as not infrequently happens, a surgeon, having made a diagnosis of disease of the appendix, operatively removes it, to find subsequently that it is grossly and microscopically normal, although he may be dismayed to find his diagnosis in error he is satisfied that after all his patient is in no way injured but rather physically improved as the result of the operation.

Operatively removed appendices run the entire gamut from normality to necrosis and gangrene. The amount of disease is sometimes so small as to occasion wonder that clinical symptoms could possibly have been produced and the number of such slightly diseased organs is by no means inconsiderable. How can such slightly altered organs manifest symptoms?

This question is commonly answered by assuming that the relation between the appendix and caecum is so close that so soon as the former becomes diseased, the inflammation spreads to the latter with painful effect. That can scarcely be the truth, however, as not a few of the cases in which the appendix was found perfectly normal manifested severe symptoms, especially pain, and as frequently there was scarcely any pain, and few symptoms in cases in which the appendix was found in an advanced state of suppuration or even gangrenous. It would seem as though in the cases in which the organ was normal, the painful disturbance must have been elsewhere than in the tissue of the appendix itself, and Wilms some time ago called attention to a congenital looseness of the attach-

ments of the caecum to which he applied the term *caecum mobile*. In it, the caecum, distended by gas and intestinal contents is free to move about, and if heavy, makes traction upon the mesocaecum and mesappendix, the latter a delicate tissue not calculated to endure severe strain. It is quite possible that caecum mobile may explain some, at least, of the cases of apparent appendicitis without disease of the organ.

The appendix possesses all of the coats normal to the intestine. Its interior is lined with tall cylindrical epithelium, that dips down to form numerous glands of Lieberkühn. These secrete mucus, which appears first in the form of globules in the cells—goblet cells. The number of these glands varies considerably in different appendices. They are imbedded in a delicate fibro-vascular stroma which blends with the submucosa of similar structure, but in which are embedded a number of rounded lymphoid deposits, the solitary glands. These are quite typical, and each usually contains a germinal center.

Outside this is the circular muscular coat, beyond which is a longitudinal muscular coat, upon which the serosa is fixed. The thickness of the wall of the appendix varies in different cases, but chiefly with respect to the mucosa and submucosa and the quantity of lymphoid tissue present. Its vessels, lymphatics and nerves reach it through its mesappendix, in precisely the same manner as those of the intestine, but its more restricted function determines that it be less well provided with vessels than other parts of the intestinal tube.

It no doubt has peristaltic muscular action, the waves beginning at the tip and progressing toward the caecum, but its ability to empty itself of accumulated contents is supposed to be very limited which is probably true as it is very common to find concrements in its interior, presumably the result of fecal stagnation.

The appendix has no exemption from such infectious and other injurious agents as find their way to the intestine through the blood, or through multiplication after ingestion. It participates in the infectious diseases as is shown by the frequency with which it is found to be diseased in cases of typhoid fever. Its lymphoid follicles suffer as do those of the ileum and caput coli, and not infrequently the lesions ulcerate and perforate. Indeed in typhoid fever, the patient should be watched to see that this accident does not occur.

It is assumed that the vestigial and undeveloped character of the tissue of the appendix predisposes it above other parts of the alimentary canal to the successful colonization of micro-organisms and that such predisposition added to the stagnation of its contents is sufficient to account for many cases of disease.

Undoubtedly its most frequent disturbance is infection with resulting inflammation. If this begin through the entrance of micro-organisms from the adjoining caecum, and the tissues are invaded from within, it falls into the group known as *catarrhal appendicitis*. If it result from the admission of micro-organisms from the circulating blood, it may at once become *interstitial appendicitis*. Early stages of the former are recognized by hyperemia of the mucosa, activity of the glands with an increase in the number of goblet cells, accumulation of mucus in the interior of the organ, and the appearance of polymorphonuclear leucocytes in the stroma of the mucosa and submucosa, as well as in the

lymph follicles, which enlarge. Later there may follow some desquamation of the epithelium, and the interior of the organ may be partly filled with a mixture of mucus, red and white blood corpuscles and desquamated epithelium. If there be no obstruction by fecal concrements, this flows out but if the lumen be obstructed, it may accumulate and occasion slight distention. Doubtless many cases progress no farther than this, then clear up by resolution. But if the microorganisms be more virulent and the inflammation advance, leuco-cytes appear in the muscular tissue, and collecting in certain foci may bring about suppuration. Under these conditions the vessels may undergo thrombosis, a serious complication as it most likely results in necrosis and gangrene of the wall of the appendix in their distribution, facilitating rupture of the organ. But if no such complication arises, the suppuration alone may be sufficient to effect perforation through the weakening of the wall to a point at which it is not longer able to resist the pressure of the gases and fluids occasionally forced into it.
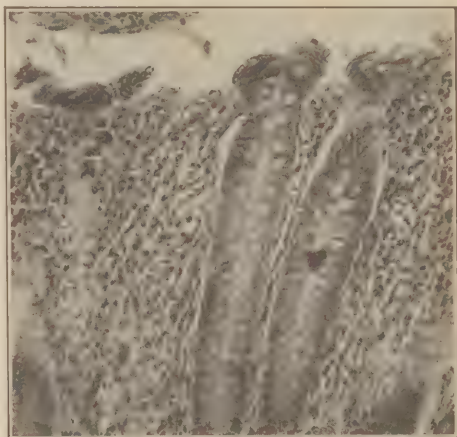
FIG. 391.—Microscopic section of an acutely inflammed vermiform appendix. The lining mucosa has been destroyed, leaving the upper end of one of the glands projecting into the lumen. The round cell infiltration extends to the internal surface. (*Photomicrograph by Prof. Allen J. Smith.*)

Among the bacteria contained in the intestine are some that immediately seize upon necrotic tissue causing it to putrefy, so that putridity—gangrenous appendicitis—is common where necrosis from violent inflammation has occurred. So wide-spread may be the suppuration as to justify the term *phlegmonous appendicitis.* Should the interior of the organ become distended by purulent accumulation, the condition is frequently described as *appendiceal empyema.* Unless the process predisposing to the perforation be exceptionally rapid, adhesions usually form between the appendix and the cecum or other near-by peritoneal surface, thereby limiting the extent of subsequent damage, and occasioning *appendicular abscess.* When no adhesions can form, intestinal contents and necrotic infectious material is distributed through the abdominal cavity, and fatal peritonitis results. Untreated appendicitis may therefore be rapidly fatal. But in most cases the result is less serious, the severity of the acute attack subsides, and resolution follows, with more or less adhesion according to the depth to which the disturbance extended. Recovery from appendicitis is, however, commonly followed by relapse, and frequently by a succession of relapses, until it becomes a chronic disease—*chronic appendicitis*—in which it is not so much the effects of the present as of the past that are to be observed when the organ is finally removed and brought for examination.

The lesions of chronic appendicitis vary considerably as might be expected, but that which is of most interest is the *chronic obliterative form.*

Presumably the condition follows an attack of the acute disease, with destruction and desquamation of the surface epithelium, and probably of most of the glands as well, about the entire circumference of some segment of the appen-

Fig. 392.—Mucocele of the appendix vermiformis.

dix. Subsequent collapse following the evacuation of the contents results in union of the approximated surfaces without regeneration of the surface covering. But there are cases in which the retention of a fibrinous exudate in the lumen of the denuded or partly denuded appendix, seems to be followed by granulation and organization of the contents through the growth of connective tissue from the mucosa or submucosa, which use the fibrinous exudate as a scaffolding for the growing cells and blood-vessels until the interior of the appendix is completely filled with newly formed connective tissue. It is, of course to be understood that in either case, the closure of the lumen of the appendix is rarely uniform and complete, but interrupted here and there. In the open lumen of an unobliterated area secretion may accumulate, there being no way for it to escape, until the distal part of the appendix becomes cystically dilated, and appears as a thin walled sac, the size of a plum or of a hen's egg, and filled with
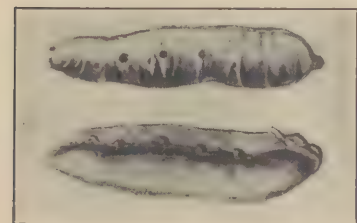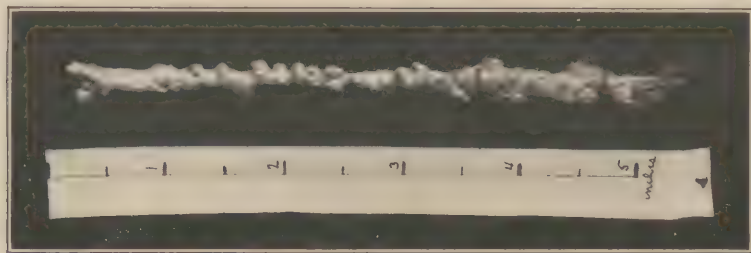
Fig. 393.—An elongated and diverticulated vermiform appendix. (*From a specimen in the Pathological Museum of the University of Pennsylvania.*)

watery mucus—*appendicular mucocele.* Or, if there be numerous alternations of patulous and obliterated segments, the retained secretion may produce a beaded or diverticulated appearance. Remnants of the glandular structure much changed in appearance by the inflammation, dislocation, and other abnormal conditions to which they have been subjected, their cells no longer regularly arranged upon a basement membrane, but slightly separated, and more or less confused with other structural elements, sometimes occur in obliterated appendices. The appearance has sometimes been interpreted to indicate impending carcinoma, but is entirely inoffensive, and benign.

For reasons easily realized, acutely diseased appendices are usually increased the chronically diseased appendix diminished in size. The acutely diseased

organs are usually free, the chronically diseased adherent through fibrous adhesions.

Tuberculosis of the vermiform appendix cannot be recognized clinically. If, however, the patient have other evidences of tuberculosis, symptoms of mild trouble in the region of the appendix may suggest it to the surgeon. It most frequently appears unexpectedly when microscopic examination is made. If, however, the lesion extends deeply and distributes the bacilli through the peritoneal lymphatics the serous surface may become studded with tiny miliary tubercles which are almost unmistakable to the naked eye. Upon opening a tuberculous appendix its inner surface is usually found to be ulcerated, the lesions being analogous with those of other parts of the intestine.

Actinomycosis and other specific infectious diseases sometimes affect the appendix, but are found unexpectedly, and have no characteristic surgical features.

Carcinoma of the vermiform appendix is probably its most frequent tumor, yet is really very rare. Curiously it assumes a remarkably benign disposition, that reverses all of the characteristics of the disease as it occurs elsewhere. About 300 cases are on record. Of these the youngest patient was a little girl aged 5 years, reported by MacCarthy and McGrath, the oldest a man aged 81 years reported by Rogg. Up to 1918 Deaver had removed 13,151 appendices in the Lankenau Hospital in Philadelphia, and among them Kelly and Reiman discovered 17 cases of carcinoma. In no case had the diagnosis been made prior to the operation, and in a number it was not made with the naked eye at all but only after microscopic examination. Of the cases the youngest was 8 years, the oldest 54 years of age.

Twelve of 16 cases whose histories were available were females—75%.

The diagnosis of acute appendicitis was made in 8 cases, of chronic appendicitis in 4 cases, and in five cases the appendix was supposed to be normal and was removed solely because the abdomen had been opened for the performance of some other operation. Practically all of the tumors were situated at the tip or at the distal third of the organ. A bulbous tip was exhibited by four. The small cell type of structure was observed in 14, the columnar cell type in 3. In a very few cases invasion and metastasis took place, but in the great majority the tumor was not heard from after the appendix was removed. The average age of the patients was 28 years, much younger than the usual cancer age. Warwick thinks that the cases can be divided into two separate groups: The spheroidal celled carcinomas that are benign, and the adeno-carcinomas that are malignant. In this he agrees with Gerlach who views the small growths in young people as *choristas*, and benign, and finds true carcinomas—adeno-carcinomas of the cylindrical cell type to be very malignant, and to occur only in elderly people, when they grow to a large size and are metastatic.

Sarcoma of the vermiform appendix is still more rare, not more than a dozen cases being on record. Both round and spindle cell tumors have been observed.

Simple benign tumors of the vermiform appendix are extremely rare.

Foreign bodies in the appendix are supposed by many to be frequent and important as causes of appendicitis. This, however seems to be a mistake. In

several thousand autopsies the author rarely observed them.   In one case he found the fragments of a cherry stone crushed by the teeth of the patient; in another a minute fragment of glass that had nearly cut through, and been the cause of adhesion between the appendix and the abdominal wall, and in still another a bristle was found lengthwise in the appendicular lumen.

Parasites, especially the adult female of Oxyuris vermicularis, are more frequent, and some have even gone so far as to suppose that this worm is the common cause of appendicitis.   There is no ground for such a statement.

THE INTESTINES

Obstruction

The movement of the intestinal contents may be stopped as the result of local inflammation with temporary palsy of some part of the muscular wall of the tube.   It is probably most frequent in acute appendicitis.   In most of the inflammatory diseases, however, the reverse is true and the patient with an acute inflammation of the intestine suffers from diarrhoea from over active peristalsis.

The obstructions to be discussed here are mechanical in nature, though so diversified in character as to make it necessary to consider them under separate headings.   They may depend upon factors internal or external.   Thus, the canal may become plugged by a mass of impacted undigested or indigestible food, as in the case reported by Eichhorst of a man whose rectum was filled by a mass of 1010 stones of cherries eaten three days before and so impacted that it was necessary to remove them a few at a time with the finger.   Sometimes the cause of obstruction develops in the intestine itself, as in the case of worms, tangled masses of Ascarides in particular sometimes so acting.   The number of worms harbored by some individuals is scarcely to be believed, as in the case reported by Pessoa, a negro boy aged six years, who under treatment expelled 558 worms.

In rare cases the intestine has been obstructed by a gall-stone of great size that ulcerated into its lumen.   Occasionally it is obstructed by a benign tumor of its wall.

But probably a greater number of obstructions are caused by mechanical conditions outside of the intestine itself, or acting through disturbances in the relations of its parts.   Of these it is necessary to speak of internal herniae, intussusception, volvulus, and strictures.

Internal Herniae

These are vague obstructions that result from the passage of portions of the bowel, usually the small intestine, through openings in the omentum, mesentery, into the foramen of Winslow, the inter-sigmoidal space, or behind inflammatory bands by which pockets are formed.   It is rarely that the exact condition can be diagnosed before operation, and it is only when the abdomen is opened that the cause of the obstruction is determined.

The actual trouble in these cases usually results from the kinking of the intestine at the margin of the opening, over which it hangs, stretched and closed by

the weight of its contents. The heavier this dragging becomes, the more the pressure tends to interfere, not only with the exitus of the contents, but also with the exitus of the blood from the veins. The less compressible arteries permit the blood to enter, but its escape is so delayed that the affected intestinal wall becomes enormously swollen, dark colored, edematous, and invaded by the bacteria, so that necrosis and gangrene follow, permitting the intestine to open, and its contents to escape, if the patient has not already succumbed to intoxication or infection.

Intussusception

This is a mechanical disturbance that usually results from the entrance of a higher portion of the intestine, the *intussusceptum*, into a lower, the *intussuscipiens*. It may be reversed and the upper portion descend upon the lower—*retrograde intussusception*. A similar disturbed relationship frequently occurs in

FIG. 394.—Intussusception in a child's intestine showing infarction of the inclosed portion. The mesentery is seen constricted in the neck of the receiving portion. (*Mac Callum.*)

unimportant degree and in multiple form in the small intestines of young children during the death agony. These invaginations, well-known to all morbid anatomists, are easy to differentiate from the more serious ante-mortem lesions under discussion, (1) because of occurrence in infants; (2) because of their frequently multiple occurrence; (3) because of their chief occurrence in the small intestine; (4) because the tissues invaginated are without signs of congestion or inflammation, and (5) because the invaginated segment is short and can easily be withdrawn.

Intussusception may occur in any part of the intestinal tract, but according to von Bergmann and Bull, 52% of the cases occur at the ileo-caecal region, 30% in the ileum, and 18% in the colon. It is much more frequent in childhood than in adult life.

The cause of the invagination and its precise mechanism are not fully understood. A few cases result from the presence of an internal pedunculated tumor,

the upper part of the actively contracting intestine, driving on the tumor which drags the intestinal wall after it. But in the majority of cases there is no such tumor, and then it is supposed by some that a part of the intestine being paralyzed or otherwise disturbed so as not to contract, an upper contractile portion descends into it. It is hard to understand how the descent could continue unless the contractile power of the lower segment revived soon after the upper entered it and then by its own contractile efforts progressively "swallowed" what had already entered. In cases occurring at the ileo-caecal region, the valve usually

FIG. 395.—Appearance of a retrograde intussusception of the sigmoid as it appeared at operation. (*Balfour*.)

descends, carrying the caecum and part of the ileum with it, sometimes to such an extent that the intussusceptum protrudes from the anus. Invaginations of the small intestine into itself sometimes reach great proportions, as in the case reported by Tracy, which was 45 cm. in length, and necessitated the resection of 210 cm. of the small intestine. In describing the specimen Tracy says "the intussuscipiens was 45 cm. in length and as 210 cm. of the bowel had been resected, the intussusceptum was therefore about 165 cm. In other words, 165 cm. of bowel had been forced into a segment of gut 45 cm. in length. The intussusception was from below upward. The cause of the lesion could not be determined." It would seem that this was an unusually large retrograde intussusception.

A more usual type is recorded by Balfour. It occurred in the sigmoid, was only about three inches long, and was caused by the presence of a malignant papillary and pedunculated tumor of the colon. The occurrence of the intussusception in this case is attributed to the presence of the tumor and antiperistaltic waves set up in consequence. The author points out that it is only in pedunculated tumors that intussusception may occur, as carcinomas, divertic-

ulitis, and inflammatory tumors involve the intestinal wall to an extent sufficient to produce a rigidity which prevents it.

When invagination occurs, the intussuscipiens dilates, and the intussusceptum contracts, with the result that the lumen of the intestine is markedly diminished; but no sooner has the condition been produced than disturbance of the circulation begins as the result of compression of the mesenteric vessels. It is frequently said that the liability and extent of invagination are determined by the length of the mesentery. That is, however, scarcely true, as the mesen-

FIG. 396.—Diagrammatic representation of the intussusception and the papillary tumor causing it, cut longitudinally. (*Balfour.*)

tery of the intussuscipiens is stretched towards the opening into which the the intussusceptum with its stretched mesentery passes. The vessels of the mesentery are therefore compressed and the return of the venous blood prevented. The result is that the tissues of the invaginated part swell more and more, and as they do so, completely close the already diminished lumen of the intussusceptum. Complete ileus, or obstruction of the bowels quickly follows, and the patient begins to vomit fecal matter and show signs of intestinal intoxication. But at the same time the congested and impoverished invaginated intestine begins to be invaded by bacteria, undergo necrosis, and become gangrenous.

Death then threatens from any one of several influences, and unless surgical intervention quickly comes the patient usually dies. In rare cases, however, things progress differently. The bacterial invasion and necrosis of the tissue, followed by its rapid death, are associated with fibrinous adhesions between the upper end of the invaginated portion of the bowel and the undisturbed portion above it, and the two are sealed. At the same time the necrotic intussusceptum begins to slough, and may be discharged from the bowel either in toto or in shreads, thus relieving the obstruction and restoring the continuity of the intestine. In such cases the patient may recover.

But this favorable result is not to be expected. Surgical intervention is the only real hope of the patient, and frequently fails as intussusception is such a rare occurrence, and its diagnosis so difficult, that in most cases retrogressive

change and infection have progressed to a point beyond that of possible recovery at the time the operation is undertaken.

The subject should not be closed without pointing out that the conditions known as prolapsus ani or recti are but modifications of intussusception, by which higher portions of the tissue of the rectum descend and project through the anus.

Volvulus

This is twisting of the intestine. It is said to occur in three possible forms. (1) The intestine rotates about its long axis for a half, three quarters or possibly sometimes a whole turn. (2) A loop of intestine twists about itself as the band of a tourniquet is twisted. (3) A loop of the intestine becomes twisted about some other portion of the intestine.

The mechanism is difficult to understand. It may occur in any part of the intestinal canal, but is said to be most frequent in the sigmoid flexure, and in individuals possessed of a long mesosigmoid. The results vary from partial obstruction with a tendency to invagination, in the case of the longitudinal twists, to complete obstruction with vascular obstruction, bacterial invasion, necrosis, and gangrene. Volvulus also occurs, but less frequently at the caecum.

In both the sigmoid and caecum one may imagine means by which volvulus may follow displacements resulting from the weight of an overloaded and distended colon, but the longitudinal twists are difficult to explain. Some years ago the author showed to the Philadelphia Pathological Society, a Meckel's diverticulum about four inches long, which was twisted upon its long axis and invaginated—combined volvulus and intussusception.

Strictures of the Intestine

These may be benign, though more frequently malignant. The former which most commonly result from the healing of ulcerations, occur most frequently in the small intestine. If caused by dysentery, they may be in the colon. The most frequent intestinal ulcerations being typhoidal, tuberculous and dysenteric, those diseases may be supposed to be responsible for the greater number. Typhoidal ulcers, occur in the Peyer's patches, have the long diameters coinciding with the length of the intestine, and heal rather by regeneration than cicatrization, so that they rarely cause strictures. Tuberculous ulcerations most frequently occur late in the disease, and rarely recover. They increase in size in correspondence with the course of the lymphatics, i.e., around the intestine in an annular manner, sometimes reaching all the way round, and should they cicatrize must produce local narrowing. Dysenteric ulcers occur in the colon, and though they may be deep and heal by cicatrization rarely produce enough contraction of the tissues to greatly diminish the lumen of so large a tube. Syphilitic ulcerations are not infrequent in the rectum, and as extensive cicatricial connective tissue formation follows in their wake, may cause strictures that are distinctly obstructive.

In ulcerative entero-colitis, the repair after recovery, may be associated with granulation tissue outgrowths which later become covered with mucosa, and form a most unusual and perplexing complication of ridges and bridges of mucosa by which some obstruction may be effected, though no distinct stricture exists.
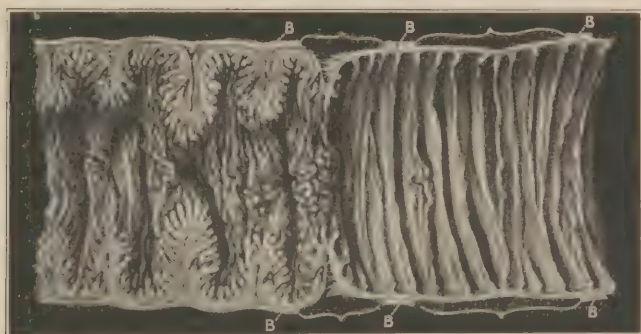
Fig. 397.—Longitudinal section of the "concertina gut." (*Welch.*)

A peculiar kind of multiple constriction was seen in a case observed by **Porter**, studied by Welch, and frequently spoken of by their friends as the "concertina gut." It was supposed by Welch that during recovery from intestinal peritonitis a thick pseudo-membrane formed upon the surface of the small intestine, to

Fig. 398.—Looking into the "concertina gut" and showing how it was obstructed. (*Welch.*)

which it was attached only at the summits of the minute ridges on the outer surface caused by the course of the arteries about the circumference of the bowel. As it was not attached to the surface of the short intervals between the ridges. its later organization and contraction drew the ridges together and caused infolding of the mucosa until the coats of the gut were transformed to a series of uniform flutings bearing some resemblance to the bellows of an

accordian or concertina. The length of the small intestine was then diminished by about 80%, and the inner projection of the folds almost completely obstructed the lumen of the bowel.

Malignant Stricture—Carcinoma of the Intestine

Carcinoma of the intestine may occur at almost any age, and affect almost any part of the small or large intestine. If seems, however, to be most frequent between the 15th and 20th years and the 50th and 60th years, the great majority of the cases occurring during this later period. It also is most frequent in the

FIG. 399.—Carcinoma of the sigmoid flexure. The specimen shows two distinct foci of carcinoma: *a* and *b* each has a depression in the center with wavy elevated margins sharply circumscribed from the surrounding healthy bowel. They are separated from one another by an interval of at least 1 cm. of healthy mucosa. (*Cullen.*)

lower part of the bowel, in somewhat this order—rectum, sigmoid, colon, caecum, small intestine. The majority of the tumors seem to begin as sessile or pedunculated excrescences beneath which the deeper coats soon suffer invasion. The excrescence sometimes grows to considerable size, tumors as large as a man's fist being not uncommon, but as is usual with malignant tumors,

degeneration and necrosis make their appearance early, infection supervenes, and the excrescence slowly disappears by ulceration, leaving a broad shallow ulcer with elevated swollen neoplasmic borders, and a densely infiltrated and indurated base. The original excrescence may cause more or less obstruction, which the subsequent cicatrization and contraction not only maintains but increases. In cases in which the tumor growth is annular, the lumen may

FIG. 400.—Carcinoma of the rectum in an advanced stage in which the tumor mass projects from the anus. (*Dr. Stilwell C. Burns.*)

almost be closed. Some cases are primarily invasive and cicatricial, assume the form of a ring of scirrhus tissue, and gradually close the lumen of the bowel without considerable ulceration.

Most of the intestinal carcinomas are cylindrical cell tumors, and many of them preserve the glandular appearance to an extent justifying the term malignant or destructive adenoma.

In some, however, the glandular appearance is not present, and the cells assume the appearance characteristic of carcinoma rotundocellulare. Mucinoid change is common in the lower bowel, and particularly in rectal tumors. Low down in the rectum squamous cell carcinoma may arise from the anus, and extend up into the rectal tissues.

The tumors may remain local for a considerable time, gradually invading the thickness of the intestinal wall and attaching it to neighboring structures by dense adhesions. Sooner or later, however they metastasize to the regional lymphatics, especially the mesenteric, and retro-peritoneal nodes ending by metastasis to the liver, and more rarely to the lung.

The disease is somewhat slow in course, the patients living two, three four and five years from the time of discovery. The rectal tumors are probably slowest to destroy life.

Infection of the ulcerated tissue is inevitable, and accelerates its destruction. A generalized infection is rare. Pockets in the ulcerated tissue become packed with feces, and the necrotic tumor forms a stinking and gangrenous mass, fragments of which occasionally loosen with more or less resulting hemorrhage. It is the occurrence of the hemorrhage that may first attract the patient's attention. In many cases he believes the trouble to be hemorrhoids, does nothing, and valuable time is lost. If the tumor can be recognized early and removed before it has spread into the adhesions, or given metastasis to the retroperitoneal lymph-nodes, life may be saved in a few, and greatly prolonged in all cases by surgical intervention.

Inflammatory sinuses sometimes run for considerable distances into the surrounding tissues, where abscesses may occur. Perforation of the bowel is, however, unusual. In inoperable cases, the formation of an artificial anus may prolong life. Death may result from the combined effects of intoxication following retention of the fecal matter, the increasing infection, hemorrhage, and the development of secondaries in the liver. It is, however, but rarely that the secondaries in the liver assume great importance. In a few cases death results from perforation of the bowel and resulting peritonitis. Occasionally the disease spreads widely over the peritoneum causing the formation of multitudes of small cancer nodules upon the peritoneal surface of the intestine, the mesentery, the omentum and the inner surface of the abdominal wall—abdominal carcinosis. This is supposed to be partly due to the distribution of the cancer cells through the lymphatics and partly to their implantation into tissues they have reached after being liberated into the abdominal cavity as the result of the softening and ulceration of the peritoneal surface. Cases with this complication usually suffer from more or less marked ascites.

Sarcoma of the Intestine

The tumors included under this name are rare. Crowther, in 1913, found the following 191 cases of "sarcoma of the intestines" in the literature:

Small round cell sarcoma	68
Lympho-sarcoma	48
Spindle-cell sarcoma	22
Myo-sarcoma	7
Melano-sarcoma	5
Fibro-sarcoma	4
Large round-cell sarcoma	3
Myxo-sarcoma	3
Endothelial cell sarcoma	3
Polyform cells	2
Mixed cell	2
Fibro-myxo sarcoma	2
Osteo-sarcoma	1
Unclassifiable	21
	191

After carefully going over them Graves, came to the conclusion that 119 of the cases collected by crowther belonged in the group of lymphoblastomas, and by another review of the literature was able to bring up the total number of reported cases of that variety of tumor to 246, adding three of his own, 249 in all, and making *lymphoblastoma* the most frequent form of "sarcoma" of the intestine. This tumor occurs at all ages from one year to eighty. It may be situated at any part of the intestinal tract, but is most frequent in the lower part of the ileum. It forms single or multiple nodular thickenings by which the mucosa, and sometimes the sub-mucosa are elevated so as to effect partial obstruction, and from this beginning, which suggests that the tumor arises from the lymphoid deposits of the intestine, it invades the outer coats, including the muscle. As the tumors grow larger they frequently become annular, and obstructive, and the elevated mucosa ulcerates, so that hemorrhage frequently occurs. Considerable lengths of intestine may become involved, and in certain positions, as, for example, the ileo-caecal region, moderate degrees of invagination may occur.

The regional lymph-nodes are usually enlarged, metastasis to the liver and more distinct viscera is not uncommon. In some cases the growth of the tumor is associated with more or less hyperplasia of the fibrillar connective tissue, so that the tumor may be firm in consistence when young and fresh, or firm and scirrhus when older. To the naked eye the tumor masses are indefinitely circumscribed, more or less homogeneous in substance, tabular in form, whitish, grayish or reddish in color. Under the microscope their structure is very simple, consisting entirely of multiplying and invading lymphocytes, in the midst of a delicate stroma.

In a few cases the tumor seems to have been cured by operative removal, but in a greater number it has returned, and it usually results fatally for the patient. Death is caused by the combined effect of the obstruction, the infection following the ulcerations, the hemorrhage, and the metastases.

The other varieties of sarcoma of the intestine are so miscellaneous in gross appearance, in histological structure and in distribution as to baffle description. Melano-sarcoma is said to occur only in the rectum.

Benign Tumors of the Intestine

In about the order of frequency these are the lipoma, fibroma, myoma, angioma and lymphangioma. The first three usually assume the form of internal tumors, the lipoma arising in the submucosa, the fibroma from it or the submucosa, the myoma, from the muscularis. The latter may be either internal or external, according as it arises from the inner or outer muscular coat. When these tumors are internal, they appear either as sessile or pedunculated nodular formations of small size, though occasionally large enough to cause more or less obstruction, or lead to invagination. If external, they form sessile or pedunculated growths that are usually small, but may reach the size of a man's fist, and do damage by their weight, the traction causing displacement, and sometimes producing volvulus.

39

Fibroma, lipoma and myoma of the internal variety are most frequent in the small intestine; lipoma of external form, is more frequent in the large intestine, where it seems to arise chiefly through excessive development of the epiploic appendages.
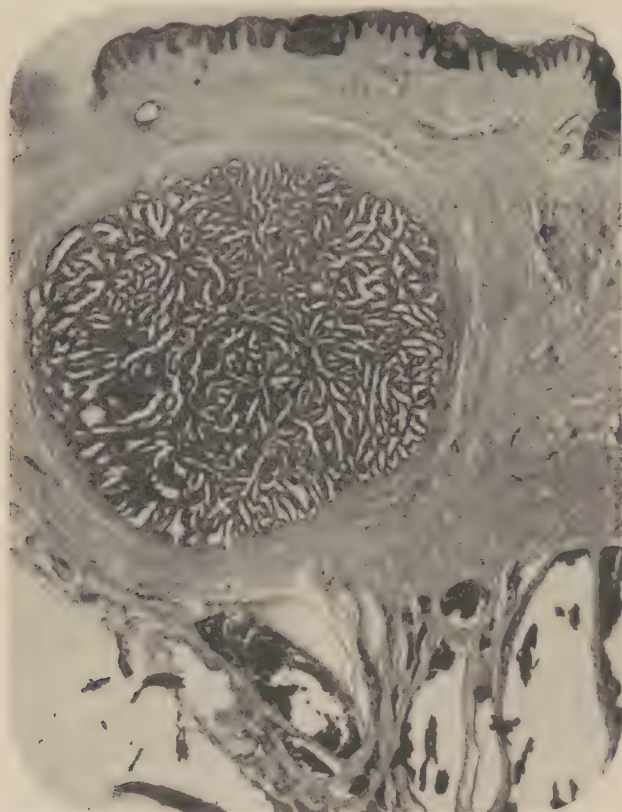
FIG. 401.—Small adenoma (?) about the size of a pea near the surface of a hemorrhoid.   (*Pennington.*)

Hemangioma and lymphangioma are very rare, seem to occur in any part of intestinal canal, and are sufficiently characteristic to require no particular description or discussion.

DIVERTICULA OF THE INTESTINE

One of these is congenital, the Meckel's diverticulum and has already been mentioned. Occasional small acquired diverticula having no definite localization, and frequently occurring upon the convexity of the organ and usually not larger than the tip of the finger, are supposed to result from imperfections of the muscular wall which permits the mucosa to prolapse, and form a pocket covered only by the serosa.

There are also rare, small, diverticula, usually of pea-size but in very rare instances reaching the size of a small apple, that arise from points near the mesenteric attachment, through prolapse of some or all of the coats of the

intestine along the course of the larger veins of the mesentery. These may occur at any segment of the intestinal canal.

But the most frequent acquired diverticula occur in the lower part of the colon, usually the sigmoid. They are pseudo-diverticula not being composed of all of the intestinal coats, the muscularis commonly being defective. Their size varies from a pea to a hazel-nut. They are usually multiple, arranged in

FIG. 402.—Upper jejunum, showing the three diverticula. (*Balfour.*)

series along each side of one of the longitudinal bands of muscular fibres, and project externally at regular intervals where vessels well supported by fibrillar connective tissue occur.

The number and regularity of their distribution is suggestive of some congenital defect in the structure of the intestinal wall. Each contains a small rounded mass of plastic or firm feces by which it is distended. Such diverticula are frequently and unexpectedly discovered at autopsy, in patients uninjured by their presence. They may however, be a source of danger when the seat of inflammation—*diverticulitis*. But acquired diverticula are not confined to the sigmoid, as has already been shown, and may occur in any part of the intestinal canal, and be very numerous, Hahnsemann having observed a case in which there were 400 separate sacculations. Although most numerous and most frequent in the sigmoid, they occasionally occur as far down as the rectum. They may be true diverticula, i.e., be surrounded by all of the intestinal coats, under which circumstances they usually do no harm as the contraction of the muscle in their wall enables them to discharge their contents. But ordinarily they are false diverticula, which McGrath describes as "mucosal hernial," because they consist only of the internal mucous membrane and the external serosa. They are really pressure diverticula, whose development results from the pressure of

gas and feces upon an imperfect intestinal wall, the weakest spots in which yield in the direction of least resistance, which is usually toward the mesentery, or into the epiploic appendages. They have been observed at all ages but are very rare except in later life, and Masson states that diverticulitis "is essentially

Fig. 403.—Symptomless diverticula of the sigmoid. (*W. J. Mayo.*)

a disease of middle life and old age." Of 116 cases operated upon for diverticulitis in the Mayo Clinic up to 1921, 81 were males and 35 females. The youngest patient was 15, the oldest 75 years, the average age 52 years.

In all cases of diverticula the patient can be considered to be menaced first by infection and inflammation of the wall of the pouch, and second by possible rupture of the thin wall of the diverticulum when the gas pressure in the affected part of the intestine is greatly increased. W. J. Mayo quotes "a certain practitioner who is also an automobile enthusiast as referring to diverticula in the colon as 'blow-outs of the inner tube.'"

Infection probably begins, much as in appendicitis, as catarrhal disturbance of the interior, but the thinness of the diverticular wall determines that peridi-

verticulitis quickly follows. This may result in the formation of an abscess, whose rupture into the peritoneal cavity is prevented by previous adhesion between the affected part of the intestine and neighboring structures. Thus the sigmoid becomes attached to the bladder, other parts of the intestine, or even to the abdominal wall. The resulting abscess is, therefore circumscribed, and the future damage limited. But the continued internal pressure directs intestinal contents into the abscess cavity, and maintains the inflammation and suppuration, commonly determining that eventual rupture shall occur into the bladder, or elsewhere. In this manner various fistulas may arise, singly or otherwise according to the number of diverticula involved. Mayo has operated upon a case in which there were six intercommunicating intestinal fistulas with one or more openings into the bladder.

The massive adhesions resulting from the attempted healing in such a condition may easily be mistaken for carcinoma, and is, no doubt, in some cases associated with it. Those most familiar with the changes in diverticulitis are most positive in their belief that the chronic inflammatory disturbance associated with it is a potent factor in initiating the cancer process. And it indeed seems probable since 14.65% of the cases in the Mayo Clinic series were found to have malignant changes at the time of operation.

Fistula in Ano

In diverticulitis of the rectum, and in various ulcerative conditions of that part of the intestinal canal, the propulsive contractions express small quantities of infective fecal matter through the diverticular orifice, or through the tissues weakened by the ulceration, so as to produce an abscess in the surrounding tissues. According to the altitude at which they occur these are known as ischiorectal, and anal abscesses, but are to all intents and purposes identical with those similar lesions occurring about the sigmoid. Such lesions are extremely indisposed to heal, because of the mechanical conditions peculiar to the parts engaged.

Thus, should there be a tendency for the contents of the abscess to escape into the lumen of the rectum during the periods of its quiescence, they may be interrupted or reversed through the occurrence of a cough or sneeze, and the infectious matter be driven back even more deeply into the abnormal space.

The result is that a long suppurative tract—a *sinus*—forms, one end of which opens into the rectum. It is also frequently spoken of as a *blind fistula*, i.e., without an external opening. Such tracts may become complicated and variously branched as the suppuration burrows more and more widely through the cellular tissue surrounding the rectum. In some cases the inner opening may heal, though the pus continuing to burrow, finds its way to the exterior, and discharges, leaving a sinus or fistula blind internally. In perhaps the greater number of cases the tract will be found to open both internally and externally, so as to be complete and then form a *true fistula*. Whether the internal opening be low down or high up, the external opening is usually quite close to the anus, but may be remote, and indeed sometimes as far away as the neighborhood of the great trochanter.

Complete fistulas cannot heal. They are continually receiving new infectious material under pressure, and eventually passing it through the abnormal external orifice. Rather do they tend to become worse and multiply, for as the infection spreads, there is a constant tendency to the formation of additional tracts that behave as the original one did. The whole ischio-rectal region therefore tends to become penetrated by fistulous tracts more or less communicating with one another, and the chronicity of the disturbance tends to the production of more or less scar tissue that detracts from its normal softness and distensibility. In such cases the condition of the patient becomes deplorable as the lower part of the rectal mucosa loses its nervous sensitivity, and gives no information to the muscle of the presence of feces and the rigid tissues cannot expand to accommodate it, so that there is incontinence of feces unless so much new formation of connective tissue have occurred as to form a stricture.

The only treatment of avail in such cases is the laying open of all of the tracts of suppuration, which then compelled to heal by granulation from the deepest part to the surfaces, eventually close permanently. But if the beginning of the lesion was a tuberculous ulcer of the rectum, healing may not take place unless the tuberculous tissue be dissected out or otherwise destroyed. The probability of this origin should always be taken into account in cases of fistula in ano in patients with evidence of tuberculosis of the lungs.

Untreated fistula in ano may be fatal, either because of accidental perforation of the peritoneal cavity, because of the prolonged suppuration, or because of association with cancer. Cancer with its accompanying infections and following ulcerations may be the cause of fistula; fistula with the resulting chronic irritation may lead to the occurrence of cancer.

THE BONES

Regeneration of Bone

When a bone is fractured, damage is always done to the related soft parts whose tissues are torn, vessels opened, and component fibres separated. The periosteum and endosteum are separated for a short distance from the ends, and between the fragments there is more or less hemorrhagic detritus. At the end of a day or two, if the injured part is kept at rest, the red blood corpuscles begin to disintegrate, the scattered cells and fibres of the soft tissues to degenerate, and phagocytes of various kinds engage in scavenging the area. About the same time the fibroblasts of the periosteum and endosteum begin to multiply actively, an exudation of serum and fibrin collected at the seat of injury furnishing a foundation upon and into which they grow. Shortly, angioblasts begin to extend from the vessels of the periosteum and endosteum and from the tiny vessels of the Haversian canals, and the growing cellular tissue assumes much the appearance of granulation tissue. It is soon present in considerable quantities, filling in the interval between the ends of the bone, surrounding it, and penetrating for a short distance into its medullary cavity. The fibroblasts which in no way differ in appearance from those ordinarily seen in the process of repair, soon change slightly in size and shape, and become iden-

tified with the osteoblasts, or inner cells of the periosteum, by which the bone was originally formed, and by which its growth is maintained. Assuming their normal function, these proceed to give off the osseo-mucin—the organic ground work of bone formation—and become separated more and more widely, as, at the same time salts of lime and magnesium are deposited, and an amorphus mass of bony texture is formed. Regularly and continually, the cells transform the whole tissue mass into an osteogenetic and finally into a temporary osseous tissue that goes by the name of *provisional callus*, and serves to support the tissues during the final stages of repair. That part of it that ascends and descends in the medullary cavity of the ends of the fractured bone is known as the "pin-callus," that part that lies between the ends of the bone, as the "intermediate callus," and that part that surrounds the seat of fracture, as the "ring callus." The quantity of the provisional callus varies in different cases, sometimes being so small as scarcely to support the bones, in other cases so great as to deform the part. Any splinters and small fragments of the bone caught in the callus are slowly absorbed, through the activity of large giant cells or osteoclasts. The provisional callus does not give sufficient strength to the bone to render it functionally serviceable, but serves to "splint" it until further progress is made.

If the extremities of the fractured bone are permitted to move, more or less cartilage may be deposited between them, but it is not constant or important in the repair of the bone. With the scavenging of the tissue, the restoration of the continuity of the periosteum and endosteum, and the vascularization of the callus, the final stages are reached. The newly formed bony trabeculae of the callus are resorbed by osteoclasts, and new bone laid down in lamellae according to the regular plan of bone formation, the deposition and absorption taking place several times if necessary, the formed bone each time becoming more regular in structure and more dense in texture, until the continuity of the ends of the shaft are reestablished, the medullary cavity above made to communicate with that below, and the external surface smoothed and rounded, to an extent that may make it difficult to detect that a fracture had occurred. The fracture is commonly said to have repaired after a few weeks, when the bone is again sufficiently rigid to enable it to perform its function, but the final finish as described above may not be accomplished until after a lapse of years.

The rapidity with which bony repair occurs varies with the age of the patient, the nature of the lesion, the freedom from complications, the physical condition of the patient, and various other circumstances. Fractures within the capsular ligament, as in the case of the neck of the femur, may be unable to heal at all because the synovial fluid prevents the formation of the necessary provisional callus. Cases in which difficultly absorbable soft tissues—tendons etc.—become introduced between the ends of the bone, may postpone healing for a long time. Healing takes place much more rapidly in youth than in later life, and in very old age, the regenerative process may disappear. Various constitutional diseases may defer or prevent healing. Movement of the fragments may not only prolong, but entirely prevent healing, and through the introduction of cartilage between the ends of the bone, and the formation of a fibrous union

instead of a bony one, lead to the formation of a new joint, *pseudarthrosis*, or *nearthrosis*. In such cases the new joint may be quite perfect, one end slightly rounded fitting into the other that excavates to accommodate it, so that a kind of head and cavity are formed, the ends covered with cartilage, and surrounded by a capsular ligament. A limb with such a joint is naturally disabled, but may be useful.

But the greatest complication associated with the repair of bony fracture is infection. It may postpone union, prevent union, destroy the bone, bring about chronic disease of the bone, or destroy the life of the patient.

Before the various results of bone infection can be satisfactorily understood, however, it is necessary to become familiar with certain of the activities of the periosteum and endosteum, both of which are bone forming tissues.

The periosteum of adults, like the pericranium of the embryo, is capable of producing bone, layer after layer without any previously modelled cartilaginous pattern such as one finds in fetal bone.

It has already been shown—see Cephalohematoma—that if the pericranium be elevated from the bone by a layer of escaped blood, it continues its function of bone formation in its new position, so that the margins of the hemorrhagic area become surrounded by a circle of newly formed bone. It will be remembered, however, that so soon as the blood is absorbed, the new bone becomes absorbed. The repair of bone as described above depends upon the activity of cells derived from these membranes.

In the shaft of a long bone, say the tibia, be struck and injured so that hemorrhage occur beneath the periosteum, the effect may be similar to what has been described in cephalohematoma. Beneath the periosteum, and above the hemorrhage—if it endure long enough—a layer of bone may be formed. Later when the hemorrhage has disappeared, the bone may be absorbed and the surface of the bone smoothed off again. Should the cause of the elevation of the periosteum be more enduring than the hemorrhagic extravasation, layer after layer of new bone may be formed. If, as the result of accident or disease the periosteum be partly torn to shreds that remain in a fairly healthy condition, irregular bony masses may be formed, and if badly dislocated give rise to curious and even fantastic bony excrescences and prominences. The periosteum like the pericranium has the power of both building up and tearing down bony tissue and the endosteum shares the same power to a limited degree.

But the periosteum and endosteum not only form the bone, they also partly nourish it, as from each there pass into the osseous tissue many small vessels by which its cells are kept alive. The stripping of the periosteum from the bone would, therefore always be fatal to it were it not for the fact that there are those other vessels from the endosteum penetrating into its substance. Extensive divulsion of the periosteum, is, however, nearly always fatal to the bone, because of the relatively greater importance of its vessels as compared with those from the endosteum.

Bone is living tissue. So soon as it dies, it is attacked by the defensive mechanisms by which the body rids itself of useless and offensive elements, and attempts are made to absorb it.

INFLAMMATION OF BONE

Inflammation of bone is theoretically divided into *periostisis*, which arises in the periosteum, *osteitis*, which arises in the cancellous bony tissue, and *osteo-*

FIG. 404.—Large necrotic fragment of bone or sequestrum from the tibia in osteomyelitis.
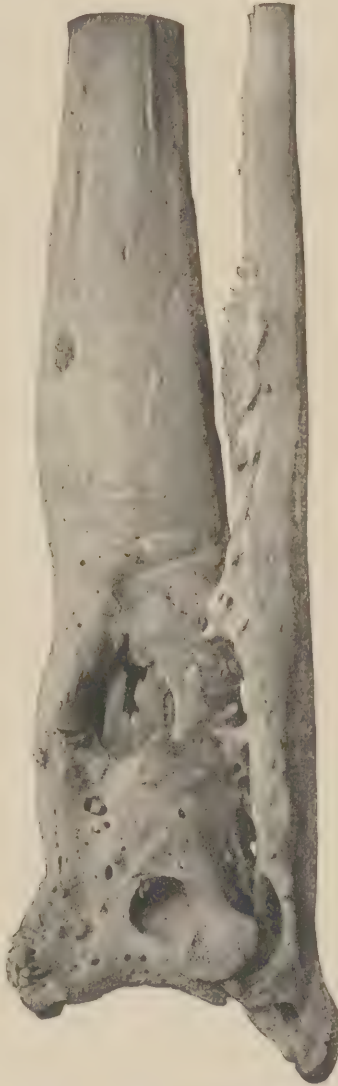
FIG. 405.—Osteomyelitis showing the sequestrum, the involucrum with orifices which represent the sinuses, and periosteal osteophytes.

FIG. 406.—Chronic periostitis with osteophytes.

(*MacCallum.*)

myelitis which arises in the medullary cavity. If the entire substance of the bone is affected, the condition is described as *panosteitis*. The disease usually

results from the presence of micro-organisms that reach the bone either through the circulating blood, or through lesions in the external soft parts.

Of the blood infections, the most frequent are caused by typhoid bacilli residual in the periosteum after attacks of typhoid fever, and by staphylococci brought from foci of suppuration in distant parts of the body.

Direct infection sometimes occurs in compound fractures, and surgical operations exposing the inner structure of the bone as well as in cases of suprajacent disease, as in chronic leg ulcers. The susceptibility of the bones to hematogenous infection seems to be greatest in youth, and to decrease with age. Direct infection through wounds may occur at any age.

The post-typhoidal infection usually takes the form of periostitis, and affects the shafts of the long bones, or the surfaces of the flat ones, rarely being severe or destructive. Staphylococcus infections and the more rare streptococcus infections localize indifferently in the cancellous tissue, the periosteum, or the marrow.

The typhoidal and staphylococcal infections usually tend to remain localized the streptococcal infections to spread. Both staphylococcal and streptococcal infection may spread, and cause phlegmonous suppuration of the entire marrow of a long bone, and sometimes distribute through the blood so as to occasion fatal generalized infection.

Inflammation of the periosteum almost never secondarily affects the joints, because it extends only to the articulating cartilage, where its invasion is checked Suppurative inflammation of the cancellous tissue of the ends of the long bones frequently does so by extension into the epiphysis, with subsequent perforation of the articular cartilage. Extension of inflammation from the bone into the joint, or from a joint to a bone, is called *osteoarthritis*.

If the inflammation be the result of the activity of micro-organisms in the periosteum the result is periostitis. Pus soon collects beneath the membrane and the subjacent bony tissue, elevating the former so as to make a shallow space—an abscess—*purulent periostitis*. The periosteum is so dense a tissue that the tendency of the pus is to spread between it and the bone, rather than to burrow outward and evacuate externally, even when the tissue to be penetrated is thin, as over the crest of the tibia.

The dissection of the membrane from the bone destroys the small vessel through which its superficial layers are nourished. If the extent of the dissection be limited, there may be enough anastomoses between the vessels of the Haversian systems, the endosteum and the more remote periosteum to maintain the nutrition. But there is a tendency for the pus to work its way into the small bony canals, compressing the vessels not otherwise disturbed, and further threatening the vitality of the osseous tissue. There is little tendency for the elevated periosteum to form new bone because the suppuration kills the osteoblasts of the inner layer, which have to be regenerated before bone formation becomes possible. If the vitality of the bone is not destroyed, and the force of the inflammation be spent, the pus may be absorbed; if the surgeon intervene and open the abscess so as to evacuate its contents, the whole process may disappear with no other alteration so far as the bone is concerned, than a slight

and temporary thickening of the membrane, which soon disappears. But if the disease spread and the dissection of the periosteum from the bone be increased beyond the point at which the nutrition of the latter is possible, some of the bony tissue dies and the first complication, *necrosis of bone*, presents itself.
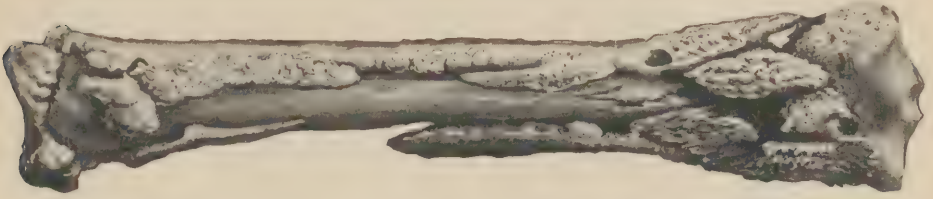
Fig. 407.—A tibia, showing necrosis of the shaft and formation of new periosteal bone
(*Bowlby and Andrewes.*)

The extent of the necrosis is usually limited to a few of the superficial bony lamellae, because the deeper layers are nourished by the endosteal vessels that have not yet suffered interruption of their function.

There is no change in the appearance of the dead lamella; they resemble the macerated bone, seen in prepared skeletons. They are smooth upon the surface, but the vessels are occluded, the cells are dead, and the chemical composition is altered, so that the adjacent living tissue resents contact with them. This is expressed in the form of bone absorption at the margins of the necrotic area, more and more osteoclasts—large and giant cells derived from the osteoblasts, engaged in the destruction of the bony tissue. As the activity of these cells succeeds, the necrotic tissue slowly separates from the living healthy tissue, by lamination. But the absorption of dead bone is tedious and time consuming, and while it is in progress other things may happen. The activity of the origially destructive process having subsided, and the pus been evacuated, the chief source of disturbance is removed, and all that remains to interfere with recovery is the presence of the fragment of dead bone to which the name *sequestrum* is applied. With the disappearance of the pus and the subsidence of the acute character of the inflammation, the osteoblasts of the inner layer of the periosteum are restored through the multiplication of their neighbors, and the boneforming function is restored. A new layer of bone, therefore, soon forms above the sequestrum, on the inner side of the periosteum, and with the passage of time becomes thicker and thicker. It incloses the sequestrum in what might be described as a tomb formed of new and living osseous tissue—the *involucrum*.

Fig. 408.—Necrosis of femur, the result of acute osteomyelitis. (*Warren.*)

But as the dead bone thus buried continues for weeks, months or years, according to its size, to undergo gradual dissolution, passage-ways—cloacae—for the escape of its transformation products are formed at occasional intervals.

The greater the size of the sequestrum, the longer it takes to absorb it and the thicker and denser become the involucra by which it is covered. Very large sequestra may be beyond the possibility of absorption so that during the entire remainder of the life of the individual the sequestrum must remain, discharging the slowly collecting transformation products through various cloacae unless surgical intervention is practiced. To assist nature in these cases is very simple, all that is necessary being to lay bare the seat of disease, chisel away the involucra by which the sequestrum is held in position, remove the dead bone, scrape away the neighboring granulation tissue, and return the periosteum to form new lamella of bone in contact with the healthy bony tissue below.

Cases in which the formation of new bone by the periosteum, begins early and is more or less continuous are frequently spoken of as *ossifying periostitis*, though not essentially different from other cases. But such excessive new formation of bone may lead to considerable deformity which may be permanent, in the sense that there is not time enough during the life of the patient for the transforming and regulating function of periosteum and endosteum to effect its ultimate renewal, and return the bone to its original perfect form.

If the micro-organisms be deposited in the cancellous structure of the articulating end of a bone, the usual phenomena of inflammation assert themselves, and the marrow spaces become filled with pus cells, which crowd out and destroy the marrow cells, and stimulate the osteoclasts, to absorb the bony trabeculae.

The leucocytes seem to have the power to assist or complete the process. Thus an abscess is formed in the bony tissue. If the inflammatory process wane before the outer compact layer of bony tissue is reached, and if the bacteria cease any longer to excite additional pus formation, recovery sets in; but if the compact layer is reached and destroyed, or if the articular cartilage is attacked and perforated, the abscess may evacuate either externally to infect the periosteum, or internally so as to infect the joint.

Recovery in cases without extension to new tissues is slow. The pus cells gradually disintegrate into amorphus granular matter, the osteoblasts of the undestroyed trabeculae begin the reconstruction of the bone which is deposited in thin layers about the space occupied by the now transforming and disintegrated pus, and a cavity is formed which in the end may appear to be empty or filled with clear fluid—a *bone cyst*.

In osteitis, the richness of the vascular plexuses in the spongy tissue make it possible that much bone may be absorbed, as the result of the suppuration, without necrosis of suprajacent or adjacent bone.

If the infecting micro-organisms directly from the blood, or indirectly from the cancellous tissue, reach the central marrow cavity of the bone, its fatty marrow quickly becomes absorbed and replaced by pus, *osteo-myelitis*. In such cases the endosteum soon becomes implicated, with effects similar to those resulting from similar disturbance of the periosteum, but confined to the inner

lamella of the bone, which deprived of nutrition, through the compression, obstruction or obliteration of their small vessels, suffer and may die, just as the outer lamella did in periostitis. But the soft character and slight resisting power of the marrow of the shaft commonly determines that the suppuration extend along considerable lengths of the bone, *phlegmonous osteo-myelitis*, so that far greater damage is usually done than when the disease begins in the periosteum. The destroyed bone becomes a sequestrum, but lies within the marrow cavity instead of upon the outer surface, and slowly becomes separated from the still living bony tissue in the same manner. Granulation tissue forms, rich in osteoclasts which attack and destroy more or less of the sequestrum, together with some of the adjacent healthy bone, until cloacae are opened, the seat of disease brought into communication with the exterior, and an opportunity afforded the morbid products of necrosis and suppuration to be evacuated. When the activity of the inflammation subsides, the endosteum, like the periosteum, forms involucra, over the sequestrum, burying it beneath new bone. For the removal of such internal sequestra, which lie in the marrow cavity, it is necessary to cut through the normal outer part of the shaft of the bone.

If the inflammation extend entirely through the bone, whether it begin in the periosteum or in the endosteum, and thus involves its entire structure, *osteo-periostitis* or *panosteitis*, results, and may eventuate in necrosis of the entire thickness of the bone, the entire shaft of the bone, or indeed, of the entire bone. Such extension of the disease is much more frequent in osteo-myelitis than in periostitis, and is very dangerous on account of the frequent fatal dissemination of the micro-organisms, staphylococci or the streptococci, through the blood of the patient.

From these brief descriptions it must be evident to the reader that the morbid conditions of the bones are largely the result of excesses, deficiencies and irregularities of bone formation and absorption following infection or other injury, and complicated by minute or massive death of the bony tissue which is difficult to remove.

Tuberculosis of the Bones

As the bones are so situated that, without a breach of continuity in the soft parts, no micro-organisms can reach them except through the circulation, and as in ordinary cases there is no such breach, or it occurs late, and as a result of the disease itself, it seems that tuberculous infection must follow hematogenous distribution of the bacilli.

In a certain number of cases it is referable to infection from the blood of the mother, and the passage of the bacilli through the placenta, as is shown by its occasional occurrence in the bodies of still-born feti.

When the disease first manifests itself shortly after birth, and, indeed, at at any time after birth, it is still possible that its specific cause was admitted to the body during fetal life. But so soon as the child is born, the general prevalence of tubercle bacilli makes it probable that they are inhaled or ingested, admitted to the lymphatics and blood-vessels, and distributed throughout the body to lodge in the bones, as well as elsewhere, and so to originate *primary tuberculosis of the bones.*

But as tuberculous lesions of the lungs and lymph-nodes are frequently found associated with those of the bones, sufficiently advanced to be contemporaneous with them, or even antecedent to them, many pathologists have come to look upon tuberculosis of the bones as secondary lesions.

But as opposed to this view may be pointed out that the lesions of the bones are usually the result of infection by the bovine type, and those of the lungs, by the human type of tubercle bacilli. Also it should be remembered that the disease occurs in childhood, when much milk is consumed, and infection from diseased cows therefore likely.

The disease usually first makes its appearance in the spongy tissue of the short bones, or the articulating ends of the long bones, most frequently the carpal, tarsal, vertebrae, upper and lower ends of the femur, and head of the tibia. Rarely in children, the phalanges, and still more rarely the temporal into which it usually extends after disease of the middle ear.

Two not very distinct varieties of the disease are described, the granulomatous, and the caseous.

Beginning in the cancellous tissue, there first forms, a lesion identical with the well known miliary tubercle. About it daughter tubercles form, those nearest together combining until a conglomerate lesion is built up. The development of the tubercles, excites stimulation of osteoclastic cells of all kinds, and the delicate bony trabeculae become absorbed, and larger spaces formed to accomodate greater tuberculous masses, thus continuing until extensive areas of the cancellous structure have been destroyed and replaced by the tuberculous tissue. With the destruction and softening there goes a certain amount of suppuration, and *tuberculous abscess* is formed.

The short bones may be thus destroyed until only a thin outer coating of bone remains, and it may be perforated by passages through which the necrotic content is eroding its way to the exterior.

In the case of the vertebrae, the strength of the bone as a support is thus lost, and the weight of the body causes the bodies gradually to yield to this pressure, so that the spine becomes curved and finally sharply angulated, with the production of the posterior "hump" of the kyphotic.

In the epiphysis of a long bone, the extension of the disease is apt to penetrate into the adjacent articulation.

In the phalanges, the disorganization of the interior of the articulating ends, followed by invasion of the marrow, and the growth of the tuberculous lesions inside of the bone, are accompanied by periosteal new formation of bone upon the exterior. But as the bone may be destroyed on the inside, faster than it is being made on the outside, the whole structure may become transformed into a barrel-shaped mass of tuberculous tissue covered by a very thin layer of newly formed bone—an appearance that suggests that the bone has in some way become inflated, and hence is known as *spina ventosa*.

Tuberculosis of the bones may begin in the periosteum, and not infrequently extends from the deeper structures to the periosteum. But the latter does not play the same important osteogenetic rôle in tuberculous osteo-myelitis that it does in the more simple forms probably because the tuberculous disease is so

destructive that the membrane disappears before it. The destruction effected in tuberculosis is slow. As the bony tissue is impressed by the growing tubercules, there is first absorption, then necrosis, affecting limited areas at a time. The result is very different from that seen in ordinary necrosis where extensive destruction is rapidly accomplished, so that great areas of bone die unchanged in appearance. The tuberculous necrotic areas are minute, for the most part, and the tiny sequestra appear as spicules and granules distributed through the general diseased mass.

Such molecular bone destruction is known as *caries*. Extension to the surface of the bone, and penetration of its superficial substance is followed by collections of puriform and necrotic matter immediately about the bone, and frequently by the local death of the periosteum. There thus forms a necrotic collection of slow formation, puriform appearance and indefinite duration—*a cold abscess*. In its neighborhood remaining semidetached strands of periosteum may form osteophytes, or may pile up new layers of limited extent and dense or even ivory consistency.

When the abscesses open externally, granulation tissue not infrequently fungates and they continue, indefinitely, to discharge a thin fluid, more or less purulent in appearance and in which gritty matter, the residuum of the carious process is mixed with flakes of necrotic tissue and miscellaneous cells—*curdy pus*.

The ultimate destruction may be great. In *coxalgia*, the head of the femur may detach, the great trochanter separate, the hip joint cavity be disorganized, its articulating cartilages destroyed. The disease may involve the acetabulum, and extend to the os innominatum from which the periosteum may be stripped, the tissues round about the joint becoming transformed into a gelatinous purulent mass whose structures can scarcely be any longer recognized.

The same kind of destruction at the knee joint, the wrist or ankle, constitute the "*white swelling*" of former times. The cold abscesses of tuberculosis sometimes burrow great distances through the surrounding tissues, to reach the surface and evacuate. In *Pott's disease* or tuberculosis located in the lower dorsal or upper lumbar regions of the spinal column, the pus entering into the sheaths of the psoas muscles, may effect their entire destruction, descending to point in the inguinal region, upon the thigh, or, in rare cases, in the popliteal space.

The periosteal tuberculosis is usually characterized by comparatively shallow superficial lesions. Such are sometimes observed upon the heads of children. The outer table of the skull is soon penetrated, and the disease extends into the diplöe. Rarely the inner table is also penetrated and the disease may then spread to the meninges with fatal result.

When a bone is cut so as to expose the tuberculous lesions to the eye, the appearance varies. In the *granulating form*, the cancellous tissue is more or less widely replaced with soft reddish, easily bleeding, granulation tissue in which it may require great care to discover gray miliary tubercles. This tissue extends widely, erodes the surface, and grows out of the various fistula, so as to fungate externally wherever there is opportunity. In the *caseating form*, the

spongy tissue is partly replaced, and the bone more or less widely invaded by deposits of grayish or yellowish cheesy substance.

Microscopically examined, these tissues show the characteristic histological picture of tuberculosis, and are, therefore easily recognized. In the granulating form the tubercles are cellular, with many easily recognizable giant cells, and with little caseation. In microscopic sections of bone, osteoclastic giant cells are normally present, and must not be confused with the larger foreign-body giant cells of the tubercles. In the caseous or caseating form of the disease, the only difference is the occurrence of wide-spread caseous change in the tuberculous tissue masses.

Secondary tuberculosis of the bones occurs in nearly every case of chronic tuberculosis of the lungs. It, however assumes the form of minute miliary tubercles scattered widely throughout the marrow and cancellous tissue, and as, in these cases, the tubercles do not tend to spread, they are of no importance.

Even without surgical intervention tuberculosis of the bones may improve and a few cases entirely recover. At least the tuberculous process becomes inactive, the destruction of the bony tissue ceases, and the condition then becomes transformed to all intents and purposes into what corresponds to simple necrosis, followed by the reparative phenomena observed in osteo-myelitis. To hasten the favorable outcome the operator endeavors to assist nature by removing the necrotic bone and morbid collections, and so to pave the way for regeneration at the same time that he places the patient under conditions generally favorable to the recovery from tuberculosis. Naturally the various deformities persist after recovery, so that many persons may be observed in every community, deformed as the result of antecedent but now inactive tuberculous disease of the bones.

But though tuberculosis of the bones is one of the most benign forms that disease assumes, its inactivity and apparent recovery are not always indicative of the complete extinction of the bacilli. Old foci of tuberculous bone disease sometimes revive and distribute bacilli throughout the body so as to be the cause of miliary tuberculosis.

Syphilis of the Bones

Syphilis of the bones has but moderate surgical interest. It has become comparatively rare with better understanding of the disease, and more thorough methods of treating it. However, when they do occur, the lesions are so striking as to be of interest, especially as exemplifying the remarkably destructive character the disease may assume if neglected.

Congenital syphilis is almost always attended by more or less bone disturbance, that best known being the osteo-chrondritis that shows as *Wegner's sign*, and is diagnostic of the condition. It is, however, of no surgical importance, and may here be neglected.

In secondary acquired syphilis the patients commonly suffer from more or less pain in the bones, and it is commonly stated that they are to be referred to periosteal disturbance attending that stage of the disease. But the evidence of any thing other than transitory swelling of the periosteum is very slight. It

may therefore be assumed that lesions of the bones are characteristic of the tertiary stage of the disease.

In a general way it may be said that the formation of the gummatous granulation tissue is the beginning of the process, that it causes the destruction that follows, and that repair goes hand and hand with the destruction, though perhaps never quite able to keep pace with it.

The lesions most frequently begin in the periosteum, and constitute the *syphilitis periostitis*. This occurs by perference in bones that are covered with thin layers of soft parts—the cranium, the sternum, the face, the shin, the clavicle, the scapula, and the phalanges. Presumably some mild traumatism explains this distribution.

The first stage seems to consist of cellular infiltration into and beneath the periosteal membrane so as to effect numerous partial separations from the bone. A primitive granulation tissue is soon formed and erodes the bony tissue, following its vessels into its depths.

Taking one of the frequent lesions upon the frontal or parietal bones, as an example, it will be found to begin as a node, or flat tabular swelling that slowly spreads extending first in this direction, then in that, and ulcerating until wide areas of the scalp are undermined, ulcerated, and soon infected. Beneath the scalp of these areas, gummatous granulation tissue follows the vessels through the outer table which becomes eroded and porous, and so reaches and extends into the diplöe. As the vessels follow a tortuous course, a very curious worm-eaten appearance of the bone is found when the pericranium is raised.

Much the same is observed when the periosteum is raised from any other bone. It will be found to be greatly changed, no longer of uniform thickness and texture, but ragged, more or less villous, and with attached processes of granulation tissue that descend into the depths of the bone. It strips easily in some parts, with difficulty in others, especially where it is soft and tears. Where removed, it leaves the bone rough, porous, and full of serpiginous and serpentine defects.

With the advent of ulceration of the surface, infection by pus cocci is certain to follow, and add to the primary syphilitic disease, secondary complicating periostitis, and later osteo-myelitis. A considerable part of the manifestations seen have nothing to do with syphilis *per se*.

The simple syphilitic destruction of the bone that takes place under the unbroken and unopened scalp is without these phenomena, and goes by the name of *caries sicca*. With the opening of the scalp by ulceration comes true and more massive necrosis. The exfoliation of the sequestra, and the deeper penetration of the gummatous tissue, eventually brings the disease to the inner table which similarly yields, so that actual penetration of the cranium may be effected over considerable areas, or at numerous points. Under such conditions, if there be no associated complicating infection, the disease may slowly spread to the meninges, and later to the brain itself. But if secondary infection be present, meningitis almost invariably results and the patient dies. In extreme cases the entire cranial vault may be thus honey-combed and worm eaten by the gummatous extensions, and many perforations occur. Under antisyphilitic

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treatment appropriately administered, the process may be checked, and repair set in. Even without such treatment the force of the destructive influence sometimes seems to expend itself and repair begin. The bony losses are not usually replaced by new bone, but by fibro-connective tissue, however, where the pericranium remains new bone may be formed about the destroyed areas, as thick rounded rims of bone as dense as ivory. Here it may be remarked that wherever new bone is formed as the result of syphilitis disease, there is a pronounced tendency for it to assume this dense form—*syphilitis osteosclerosis.*

Long years afterwards the lesions still show as depressions with slightly elevated margins, and macerated bones may show old perforations as well as osteosclerotic indurations about porous areas resembling pumice stone.

Almost as frequent as the cranial lesions are those that occur on the anterior aspect of the tibia at about its middle third. Here the general progress of events is much the same except that there being no diplöe with serpentine vessels the disease remains distinctly superficial. It results, however, in the descent of the gummatous granulation tissue along the course of the small nutrient vessels, and the erosion and rarefication of the bone, at the same time that new bone is being formed by the periosteum and sometimes the disturbed endosteum below. However, the bone is so rarely diseased all the way through, that the endosteal participation is unusual. The disturbance results is the loss of the crest of the tibia through thickening and rounding of its surface by the osteoporosis and ossifying periostitis. The anterior wall of the shaft of the tibia may be increased to three or more times its normal thickness, and made very porous and spongy. The gummatous tissue commonly ulcerates, and leg ulcers may thus result, the base of the ulcer, in contact with the diseased bone having no tendency to heal until the disease of the bone is at an end.

The well known characteristic bone deformities of syphilis, the saddle nose and the perforated palate, do not result from the bone disease described, but from the extension of syphilitic disease from the mucous membrane to the bone, and are more in line with the simple necrosis that follows inflammation and ulceration of the periosteum. They are rather complications of syphilis than an actual part of it.

Syphilitic osteitis and *osteomyelitis* are different. They occur in the spongy bones, beginning in the interior, first with the formation of gummatous granulation tissue which destroys the bone by compression and absorption, rather than by caries, and replaces it by a red uniform mass that may melt away into grayish or yellowish gelatinous necrotic matter.

In many cases this cannot be recognized until the bone is opened, but in some it extends to the compact tissue of the shaft which becomes thinned to a mere rind unable to sustain the weight thrown upon it so that the bone fractures spontaneously, or in the case of the bodies of the vertebra collapses as in tuberculosis. Or, the shaft becomes expanded by the morbid products within, and the bone deformed, especially if there be simultaneous ossifying periostitis by which new bony lamella are added externally. Under such circumstances the bone may be deformed out of all resemblance to its normal form, and unrecog-

nizable.   Rarely the central lesions effect communication with the exterior, so that extensive periosteal disease is added.

In case of doubt as to the syphilitic or tuberculous nature of any bone lesion, one should endeavor to demonstrate the respective specific microorganisms. This may, however, be difficult as they are not usually numerous.

Tumors of Bone

In Part II, which was devoted to the general consideration of tumors, the main facts regarding the tumors of bone were given as much space as the scope of this work permits.   It will not, therefore, be possible to repeat them here.

But in order that the reader may have a clear idea of their variety and relationship we introduce the following tabulation recently prepared by Ewing. after which we pass to some added considerations of the most frequent, most dangerous, and hence most important of the bone tumors, *sarcoma.*

Osteoma $\left\{ \begin{array}{l} \text{Spongy} \\ \text{Ivory} \end{array} \right.$

Chondroma $\left\{ \begin{array}{l} \text{Pure chondroma} \\ \text{Chondromyxoma} \\ \text{Myxoma} \end{array} \right\}$ $\left\{ \begin{array}{l} \text{Capsular} \\ \text{Periosteal} \\ \text{Central} \end{array} \right.$

Angioma: Cavernous

Endothelioma $\left\{ \begin{array}{l} \text{Angioendothelioma} \\ \text{Diffuse} \end{array} \right\}$ $\left\{ \begin{array}{l} \text{Solitary} \\ \text{Multiple} \end{array} \right.$

Benign central giant cell tumor and its variants $\left\{ \begin{array}{l} \text{1. Bone cyst} \\ \text{2. Giant cell tumor} \\ \text{3. Xanthosarcoma} \\ \text{4. Myxosarcoma (benign)} \end{array} \right.$

Osteogenetic sarcoma $\left\{ \begin{array}{l} \text{Periosteal (extraperiosteal)} \\ \text{Solid medullary and sub-periosteal} \\ \text{Telangiectatic} \\ \text{Sclerosing} \end{array} \right.$

Myeloma $\left\{ \begin{array}{l} \text{Plasma cell} \\ \text{Lymphocytic} \\ \text{Myelocytic} \\ \text{Erythroblastic} \end{array} \right.$

Sarcoma

Sarcomas of bone may arise from any bony structure, but most frequently make their appearance in the spongy extremities of the long bones, especially of the lower end of the femur, the upper end of the tibia, the upper and lower ends of the humerus, and the lower ends of the radius and ulna.

Their appearance usually either coincides with the period of growth, or follows injury.   Particular attention has been bestowed upon them during recent years by both Ewing and Bloodgood, and it is to their writings that we are chiefly indebted for the following facts.

I. *Periosteal or Extraperiosteal Sarcoma.*—These do not arise from the bone, but from the periosteum, and from its outer, rather than from its inner portion. From a wide-spread or circumscribed beginning the new growth spreads out over the bone, sometimes even surrounding it in an annular form.   Protected by the

FIG. 409.—Periosteal sarcoma of the middle third of the femur. (*From a specimen in the Pathological Museum of the University of Pennsylvania.*)
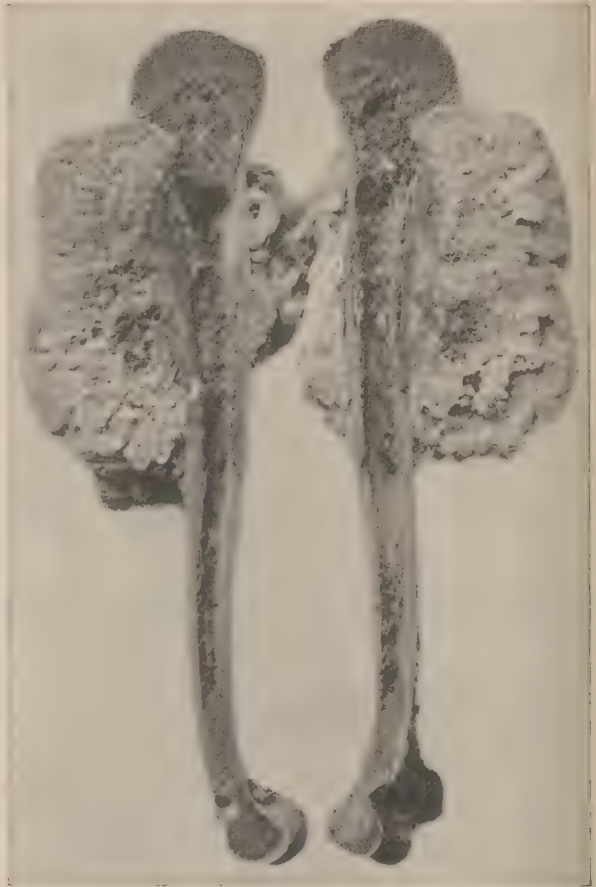
FIG. 410.—Periosteal osteosarcoma of the humerus. The marrow cavity is not invaded.   (*MacCallum.*)

undisturbed inner layer, the bone itself is usually either not disturbed, or suffers but little superficial erosion.   Only in very rare cases does the disease extend more deeply and penetrate the shaft.   The result is a more or less massive new formation, usually well circumscribed and encapsulated, by which the surrounding tissues are displaced, but which is never surrounded by a superficial shell of bone.   Any newly formed bone included in the tumor usually appears in the form of trabeculae that radiate perpendicularly from the shaft.

The size to which the tumors attain has a definite relation to the histological structure. Thus, if it be composed entirely of spindle cells it is soft, and should any mucous substance be between the cells, moist and almost fluctuating.

Under these circumstances the tumor is usually highly malignant, quickly invades the neighboring muscular tissue, and readily gives metastasis to the lymph nodes and lungs. Tumors of this variety have been known to kill the patient within six weeks after the trauma by which the growth of the tumor was determined. If, however, there be admixture of fibrillar, chondrous, or osseous tissue, showing that the cells undergo partial differentiation,

FIG. 411.—Central fibro-sarcoma of the lower end of the femur in a white woman aged 29 years. There was a history of contusion 10 months before the photograph was taken, but no swelling until 6 months later. The tumor grew rapidly and destroyed the outer shell of bone. The difficulty in making a correct diagnosis in these cases is evident from the fact that the patient lived 4 years after operation, which made Dr. Bloodgood suspect that the lesion might be osteitis fibrosa instead of sarcoma. (*Bloodgood.*)

FIG. 412.—Solid central and subperiosteal osteogenetic sarcoma; the sharp limitation at epiphyseal line may be noted. (*Ewing.*)

the invasive tendency is postponed, metastasis comes much later, and the tumor may attain to a much larger size. The greater the preponderance of

intercellular product, the larger the tumor may grow, and the longer the patient may live.   Metastasis, which is the chief cause of death, rarely occurs so long as the encapsulation of the tumor confines it to the tissues related to the bone; it comes quickly, however, when the muscles are invaded.

A roentgenogram made before operation shows the almost unaltered shaft of the bone passing through a solid and fairly uniform tumor mass, or attached to one side of it.   The tumor is surrounded by its capsule, but never by a shell of bone.

The intercellular products give added density to the tumor.   The more fibrillar are firm, those with osseous trabeculae friable, those with abundant
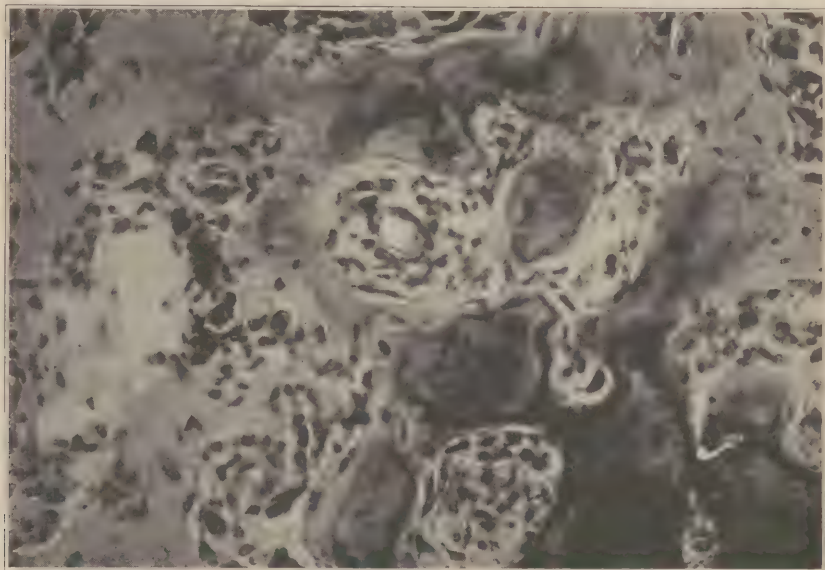
Fig. 413.—Structure of sclerosing osteogenic sarcoma; large spindle and polyhedral cells lying in osteoid and osseous tissue; nuclei large and hyperchromatic.   (*Ewing*.)

cartilage dense and elastic.   The tumors with excessive cartilage formation grow slowly and persistently and may attain to an enormous size in the course of months.   The average duration of life, however, is not much more than a year.   The tumors recur again and again when excised or amputated.

II. *Solid Sub-periosteal and Medullary Sarcoma.*—These probably arise from the endosteum of the articulating ends of the long bones, their growing cells causing the cancellous substance to become absorbed and replaced by the tumor tissue, which extends to a considerable extent into the adjacent marrow cavity before the compact osseous tissue of the shaft becomes sufficiently rarified to distend into a fusiform enlargement which is at first covered by a shell of bone representing the compact tissue of the shaft, then by a thinner layer newly formed by the periosteum, and finally by the periosteum alone which becomes thinner and thinner, until it yields and permits the tissue of the tumor to infiltrate the adjacent muscles.   Such tumors may become as large as an adult human head.

The tumors are solid and usually firm and resisting because of the admixture of cartilaginous or osteoid stroma. As in the case of the preceding, any bone formed in the substance of the tumor is generally arranged in trabeculae that more or less distinctly radiate from the shaft.

In some cases the consistency of the tumor becomes changed through the occurrence of hemorrhage or necrosis of its substance, so that parts of it may be soft or even fluctuating.

Histologically the greater part of the tumor is either composed of spindle cells or their products, and is, therefore fibroblastic, chondroblastic, or osteo-blastic, but among the spindle cells, scattered or in groups are spherical or polyhedral cells presumably descended from the bone marrow.

A roentgenogram of this form of tumor, taken before it is disturbed by operation, shows the shaft of the bone and its covering periosteum to be distended over the growing solid tumor, the outer limits of which are frequently marked by a thin bony shell. The extra-periosteal sarcoma was on the outside of the bone, and did not essentially disturb it; in this case it is on the inside and distends and eventually ruptures it.

III. *Telangiectatic Bone Sarcoma: Angio-sarcoma of Bone: Malignant Bone Aneurysm.*—These tumors seem to occur only in young people, and to run a remarkably rapid and fatal course, nearly always terminating fatally within a year, no matter what treatment is practiced. No case is known to have recovered.

From what elements of structure the tumor springs, or how it begins has not been determined, but it is a central tumor, beginning in the expanded ends of the long bones, extending along the marrow cavity, and effecting absorption and distension of the shaft, until it is reduced to a mere bony shell covered with periosteum. The chief characteristic is its extreme vascularity, which may be such as to give it a pulsatile quality and its name aneurysm. The tissue is dark colored, spongy, and hemorrhagic. Histologically it is an angio-sarcoma, the stroma of which usually consists of spindle cells. In malignancy it resembles its predecessor.

IV. *Sclerosing Osteogenetic Sarcoma.*—This is a relatively benign variety of bone-forming sarcoma. As usual it most frequently appears at the extremities of the long bones, from which it extends to the marrow cavity and periosteum transforming the bone into a massive clavate osseous formation, that may be of ivory-like hardness. The marrow cavity becomes filled with this new bone, the cancellous substance replaced by it, and the shaft either thinned and distended over it or blended with it. The periosteum usually remains stretched over the whole as a capsule, but eventually becomes ruptured, after which the softer substance of the tumor invades the surrounding structures in the form of a spindle-cell new growth.

The histological characteristics are quite distinct. There is first the formation of a fibroblastic cellular tissue, second its gradual transformation into compact hyaline or osteoid tissue, and lastly the formation of dense compact bone. It is, of course the cellular portions only that constitute the potentially malignant elements of the tumor. In them the blood-vessels are very imperfectly formed,

so that metastatic transportation of the tumor cells is easy. However, the tumor usually grows slowly, one or two years sometimes passing before the bone is noticeably enlarged, and from five to twenty-five before the fatal termination is reached.

The roentenogram is entirely dissimilar from those previously described, showing a central mass of compact bone by which the shaft is distended.

Carcinoma of Bone

Carcinoma of bone is always secondary. The primary tumor may be situated in any organ subject to the disease, but the order of frequency with

FIG. 414.—Secondary nodule from a tumor of the breast, involving upper end of femur, and producing a pathological fracture. (*MacCallum.*)

respect to secondary invasion of osseous tissue seems to be prostate, thyroid, breast and uterus. The actual invasion is generally conceded to take place through blood metastasis, though permeation may explain some cases. The aggregations of tumor cells replace the marrow, distend its spaces in the cancellous bone or fill and distend the medullary cavity of the shaft, causing absorp-

tion of the mineral salts and weakening the tissue until spontaneous fracture becomes inevitable.

OSTEITIS DEFORMANS; OSTEOMYELITIS FIBROSA; OSTEITIS FIBROSA CYSTICA; OSTEITIS HEMORRHAGICA; BENIGN BONE CYST, AND BENIGN GIANT CELL SARCOMA

Certain bone dystrophies are clinically characterized by symptoms sufficiently clear cut to enable them to be classified, though atypical cases may be assigned to any one of the denominated classes according to the opinion of the observer; pathologically they are so inextricably linked together as to appear to be but variations of the same morbid process.

At one extreme of the series, the cases merge with the general constitutional malady known as osteomalacia; at the other, with apparently purely local lesions, the benign bone cyst and benign giant cell sarcoma. The present consideration has to do with the diseases known as Osteitis deformans, described by Paget in 1877; that first described by Hirshberg in 1886, and later studied by von Recklinghausen in 1891, and called by him, Osteitis fibrosa cystica; what appears to be the same disease, studied by Barrie, in 1914, and called "Osteomyelitis hemorrhagica," and certain local disturbances of the bones carefully studied by Bloodgood in 1910, and described as "Benign bone cysts" and "Benign giant cell sarcoma."

From the pathological point of view these may be no more than different manifestations of the same process, sometimes appearing locally and remaining confined to a restricted area in a single bone, sometimes simultaneously in several bones, sometimes distributing widely over many of the bones; sometimes mild and productive, sometimes severe and destructive.

FIG. 415. —Paget's disease of the bones. (*From a patient in the Philadelphia General Hospital.*)

No cause either local or general has as yet been found to explain the lesions, which sometimes make their appearance early in childhood, sometimes not until late in life; in certain manifestations affecting females chiefly, in others males.

The degree of disability and deformity are directly proportionate to the extent and nature of the bony involvement and the particular bones affected. They may also be determined by the ability of the bones to react to the peculiar stimuli by which the changes are brought about. The more modifiable bones of youth showing changes of a more destructive character than the less active bones of age.

As the histological alterations amply explain the gross appearances, it seems well to begin the description of the pathology with them.

In the spaces of the cancellous bone, the red marrow is gradually replaced by a finely fibrillar, avascular connective tissue of a gray color, at the same time that the bony trabeculae are slowly absorbed. In the compact substance of the long bones, lacunar absorption inititates the process, which is followed by a halisteresis that transforms the compact bone into a kind of spongy substance
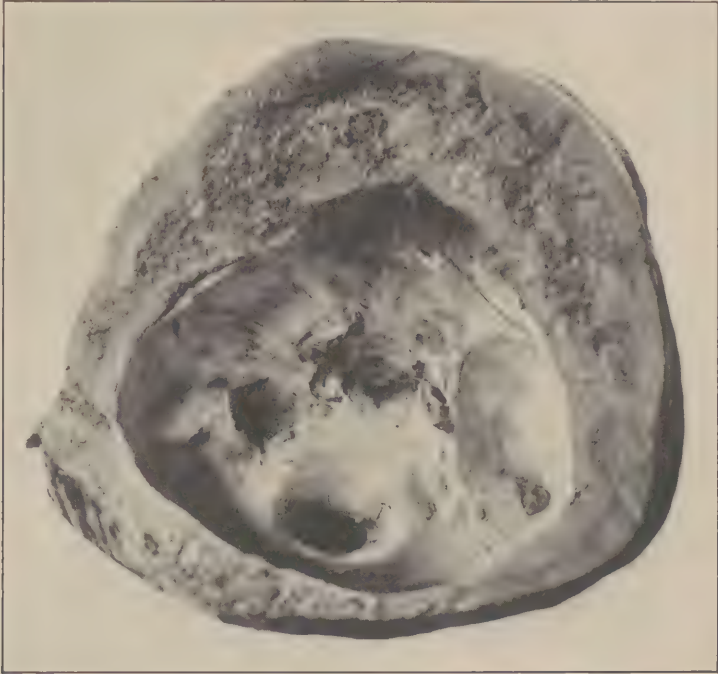
Fig. 416.—Paget's disease of the bones, showing the enormous thickening of the bones of the cranium. (*From a case dying in the Philadelphia General Hospital.*) (*Dr. Baldwin Lucke.*)

with intercommunicating spaces in which the same delicate fibrillar tissue appears and grows, extending into the shaft and causing disappearance of the fatty marrow. The bones affected thus become so weakened through loss of their mineral substance, that pathological fracture is frequent.

But if the extent of the disease be more widespread, and a greater length of the shaft involved, fracture is less frequent and the bone more commonly bends. The newly formed fibrillar tissue, poor in vessels, is prone to retrogressive change. Where it persists it becomes osteogenetic and resembles provisional callus, being filled with bony trabeculae, that some regard as metaplastic. Parts of it commonly melt away with the formation of cystic spaces filled with mucinoid-substance when young, serous fluid when older. Into the connective tissue and sometimes into the cysts, hemorrhagic extravasations of larger or smaller size frequently occur, whereupon it changes into a kind of granulation tissue rich in

giant cells, that may develop into red-brown tumor-like masses that resemble giant cell sarcoma.

The periosteum is not usually disturbed, and its osteogenetic function is retained, so that fractures may heal kindly, and the outer surface of the lesions become covered with new bone that may be dense and even eburnated.

The chief pathological features, then, are halisteresis followed by malacia; fibrosis followed by flexibility and plasticity; softening followed by cyst formation; hemorrhage followed by tumor-like granulation tissue formation; and new
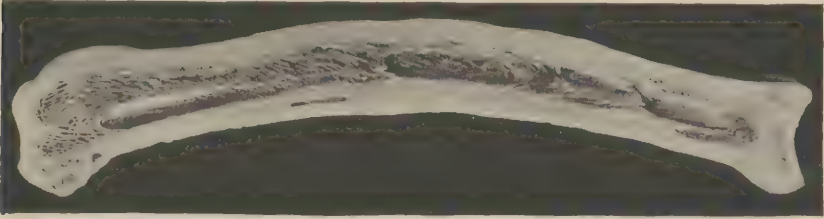
FIG. 417.—Section of a tibia from a case of osteitis deformans—Paget's disease of the bones. (*Bowlby and Andrewes.*)

bone formation resulting in hyperostosis.   At different ages, in different combinations, and in different bones, these are the sources of the differing clinical manifestations that are described as different diseases.

Thus, if the disease affect the bones of the face, fibrosis, cystic change, hyperostosis and giant cell sarcoma may lead to the peculiar massive deformity known as *leontiasis osseum*.   If it affect the bones of the cranium, the absorption of the earthy salts, followed by fibrosis, produces great thickening of the calvarium which, in cases of secondary ossification, becomes dense and hard, or in its absence may be cut with a knife, and is flexible and leathery.   The circumference of the cranium may be uniformly or irregularly increased so that the head may appear much enlarged while the face seems to be abnormally small.

If the spinal column be affected, the individual vertebrae become softened and yield to the downward pressure of the head and shoulders, so that kyphotic and scoliotic curves occur, and in bad cases, after the patient becomes bed-ridden, the bodies of the vertebrae may be transformed into a softened grayish or reddish tissue that may easily be cut with a knife.   Where the shafts of the long bones are affected there may be pathological fractures, or the whole bone may yield to the weight of the body, and curve remarkably.   This is especially true of the femora which von Recklinghausen described as undergoing the "shepherd's crook curve."   Wherever the fibrous or granulation tissue becomes excessive, larger or smaller grayish or red-brown nodes, sometimes of great size, may occur, giving the impression of tumors of the bones.   Over these the periosteum may extend undisturbed, or it may reinforce the diseased tissue with a thin dense bony shell.

In the cases known as Paget's disease, which progress slowly and steadily, the malacia and fibrosis preponderate; there are no tumors, and cysts if present

are few and of small size.   The result is thickening and bending of the bones without other important changes.

This form of the disturbance most frequently occurs in advanced years, suggesting, as has been said, that the general inactivity of the bones of age may have something to do with the quality of the lesions.

FIG. 418.—Three views of a patient with osteitis fibrosa cystica, showing the marked bowing of the femurs with shortening of the right leg and equinus position of the right foot. (*Morton.*)

In the more destructive form of disturbance described by von Reckling-hausen, the patients are young, nearly all less than thirty, so that the lesions appear during the period of bony activity.   In these cases the fibrillar tissue tends to form nodes, to undergo colliquation, and to suffer from hemorrhages so that cysts and giant cell tumors appear.

But the youth or age of the patient rather determines the course of the lesions than their extent or distribution. Coming late in life, the fibrosis and bending of the bones characteristic of Paget's disease may escape detection unless sufficiently wide spread to produce deformity; coming earlier, and being more destructive in tendency, the von Recklinghausen's disease attracts attention through pathological fracture of some particular bone, through marked bending of certain bones, through cystic enlargement or through the occurrence of benign giant cell-sarcoma. At the time that these seemingly local disturbances are attracting attention to the non-diseased bones, there may be less important

FIG. 419.—Skeleton of Case VI in von Recklinghausen's original paper 1891, showing characteristic skeletal deformities.

lesions in other bones that escape attention unless an examination by the X-rays be made. All of the lesions do not seem to assume the same degree of importance; some of them may remain undiscovered and recover through hyperostosis after more or less fibrotic and cystic change.

The cystic change of the newly formed connective tissue, so characteristic of the juvenile cases may come on at any time, hence there may be but one cyst of a single bone, or a congeries of cysts in a part of a single bone—Bloodgood's benign bone cysts,—or there may be wide-spread cystic disturbance of many bones. The individual cysts may be small, or as large as hen's eggs and may be filled with mucoid jelly, or with clear serous fluid. The larger and older cysts have smooth shining walls, that are said to be without an endothelial lining.

Hemorrhage may take place into the fibrillar tissue, in minute or massive form. The cause of the former is not known, but the latter are usually explained as resulting from accident. It was their prevalence that led Barrie to suppose them to be of prime importance, and responsible for the associated changes, and led him to call the disease *hemorrhagic osteomyelitis*. Before him, von Reckinghausen has looked upon the disturbance as inflammatory, and at one time called it *osteomyelitis fibrosa*. If inflammation has anything to do with the process, it must be of the chronic productive type, for there are no signs of antecedent acute inflammation, and there are never any inflammatory cellular infiltrations other than can readily be explained as secondary.

FIG. 420.—Femur and ulna from Case V in von Recklinghausen's original paper in 1891. The femur shows the characteristic bowing and the "shepherd's crooking" of the neck and head; a large cyst in the white connective tissue replaces the bone; the ulna shows three cysts and fibrosis.

But the hemorrhages are of great importance as they seem to be the source of the giant cell tumors. Such giant cells as occur in small numbers, here and there, in the fibrillar tissue, have been regarded as osteoclasts. But they more regularly occur in groups where dark points follow minute hemorrhages, and in immense numbers where there have been large hemorrhages. They also occur in great numbers about the walls of cysts into which hemorrhages have occurred. The cellular tissue in which they are contained, at first glance resembles spindle cell sarcoma, but when carefully studied is found to be a form of granulation tissue. It is well vascularized, and contains the usual miscellany of cells found in granulation tissue. The giant cells, themselves, are foreign body cells whose presence is explained by the erythrolytic and osteoclastic products disseminated through the tissue.

Morton believes the roentgenogram to afford great assistance in the differentiation of the different varieties of bone disease, and thus describes that of Paget's disease:

Paget's disease is to be recognized by the presence of a rough irregular periosteum; tremendously thickened sub-cortical bone, two or three times normal; marrow space mottled, cloudy, furred, smoky appearing shadows, generally distributed over the whole bone, even to the epiphyses and joint surfaces; smooth bones with even curves; well-healed fractures, when any occur; marked thickening of the calvarium and cystic spaces rarely more than 1–2 cm. in diameter.

It seems proper to make a brief mention of three particular clinical varieties which, it must be remembered, may be three distinct diseases.

I. *The Benign Bone Cysts.*—In 1910 Bloodgood published a collection of 89 reported cases, of which 69 were considered to be related to fibrous osteitis. It seems unnecessary to dwell further upon them.

II. *Paget's Disease.*—This condition, also called *osteitis deformans*, almost always occurs after the 40th year of life. Indeed most cases occur after 50, and many cases not until between 70 and 80. Of the 48 cases observed by Socke,

FIG. 421.—Roentgenogram of the elbow of a young colored woman with osteitis fibrosa cystica, dying in the Philadelphia General Hospital, and autopsied by Dr. Baldwin Lucke. There were many large tumors and cysts of the bones similar to that shown, and the skeleton was remarkably deformed and the patient completely disabled and bed-ridden in consequence.

the average age at the time of the onset of the disease was $45\frac{1}{2}$ years, and 57 at the time of coming under observation. The youngest patient was 28 years old. It is somewhat rare, and in a review of the literature made in 1911 by Higbe and Ellis, only 158 cases were found, including some that may not have been authentic Seventy-five per cent of the patients were men. E. A. Socke saw, personally, 48 cases in 20 years, of which 58% only were males. It usually affects the

bones, of the lower limbs, the cranium, the clavicles, spine, radius and jaw. The bones lengthen, thicken and bend, but they rarely fracture.

Morton states that the disease progresses slowly and steadily, not by fits and starts, that the cysts are small, and that the skull is frequently affected.

FIG. 422.   FIG. 423.

FIG. 422.—Osteitis fibrosa cystica of the left tibia of a patient 11 years old. Fractures occurred at 1 and 6 years. The cystic areas are distinct and invade the cortex as well as the medulla, causing a bulging deformity of the bone. (*Meyerding.*)

FIG. 423.—Right humerus showing fibrocystic disease; osteitis fibrosa cystica (?). (*Meyerding.*)

Paget himself describes the deformities following advanced cases as follows:

The most characteristic features are the loss in height, indicated by the low position of the hands, the stooping with round shoulders, the head held forward with the chin raised and the chest sunken toward the pelvis, the abdomen pendulous, the curved limbs held wide apart, and usually with one advanced in front of the other, and both with the knees slightly bent, the ankles overhung by the legs, and the toes turned out. The enlarged cranium, square looking and bossed, may add distinctness to these characteristics, and they are completed in the slow and awkward gait of the patient.

III. *Von Recklinghausen's Disease - Osteitis Fibrosa Cystica.*—This is characterized by occurrence in early life. Practically all of the reported cases were under 50 years of age, and the great majority of them under 30. As cysts have been observed in the bones of infants of 18 months, it is not impossible that this form of the disease may have its beginnings very early.

The far greater number of cases are females. All of the bones may be affected, and the number of bones involved is usually considerable. The lesions are destructive and extensive, embracing malacia, fibrosis, cystic degeneration, giant cell tumors and hyperostosis.

In 1922 Morton described a case, and made an analytical study of 63 others collected from the literature. His classification which follows, we are glad to adopt, except that instead of excluding Paget's disease from group IB2, it seems to us to be exactly where it should appear. In regard to the matter, Morton says that group IB2 is difficult to differentiate from Paget's disease "on account of having thickening of the skull." That does not seem to be a sufficiently weighty character upon which to exclude cases having so much else in common.

Group I. Without giant cell sarcoma. Of these he found 37 cases in the literature.
    A.   With cysts, fibrosis and tumors, but no marked malacia.
        22 of the above 37 cases fall into this class.
    B.1. With cysts, fibrosis, tumors and marked malacia.
        8 cases fall into this class.
    B.2. With cysts, fibrosis, tumors, malacia, and hyperostosis.
        7 cases are referred to this class. From it he excludes Paget's disease, which we think belongs to it. If they had been admitted, there would be the additional 158 cases of Higbe and Ellis.
Group II. With giant cell sarcoma. Of these he found 26 cases in the literature.
    A.   With cysts, fibrosis and tumors, but no marked malacia.
        5 cases fall into this class.
    B.1. With cysts, fibrosis, tumors, and marked malacia.
        16 cases fall into this class.
    B.2. With cysts, fibrosis, tumors, malacia, and hyperostosis.
        5 cases are assigned to this class.

The roentgenogram of osteitis fibrosa cystica as described by Morton is said to be typical. The only conditions that might be confused with it are osteomalacia and Paget's disease. In the first place, the periosteum does not take part in the disease, and is smooth and normal in outline except at fracture places where it often heaps up a well-marked callus. The epiphysis and joint surfaces also tend to remain unaffected. The cortex and marrow cavities show well-marked changes; the latter show widening and irregularity in outline, and in places a mottled appearance, with here and there clear spaces which do not seem to have any calcium content. The cortical bone is also irregular, mottled and in places thinned to a few millimetres or destroyed. It is impossible at times to tell where the cortex leaves off and the marrow cavity begins, the process becomes so confluent. The whole bone picture is also striking because of the washed out calcium content, which gives a general translucence and a honey-combed picture when cystic changes have occurred. Occasional cystic cavities show fine septal bridges making compartments which some of the French observers compare to the cut surface of a tomato. Taken as a whole, the translucence of the bone, the irregular rarified patches and long porous streaks, the enlargement of the marrow spaces and the replacement of the cortical bone and its lack of definition from the marrow cavity, constitute a picture not liable to be mistaken for any other condition. The bony deformities are marked and the bones are angulated where fractures have occurred so that a

smooth curve is not the usual finding. The bones show expansion and rein-
forcement on the convexity of the cortex, but the latter, never of marked density.

There is no treatment yet known, by which the metabolic disorder that seems
to be at the bottom of these disturbances, can be interrupted.

Such fractures as occur from time to time, must be treated as ordinarily,
unless they afford an opportunity for surgical attack upon the diseased bone,
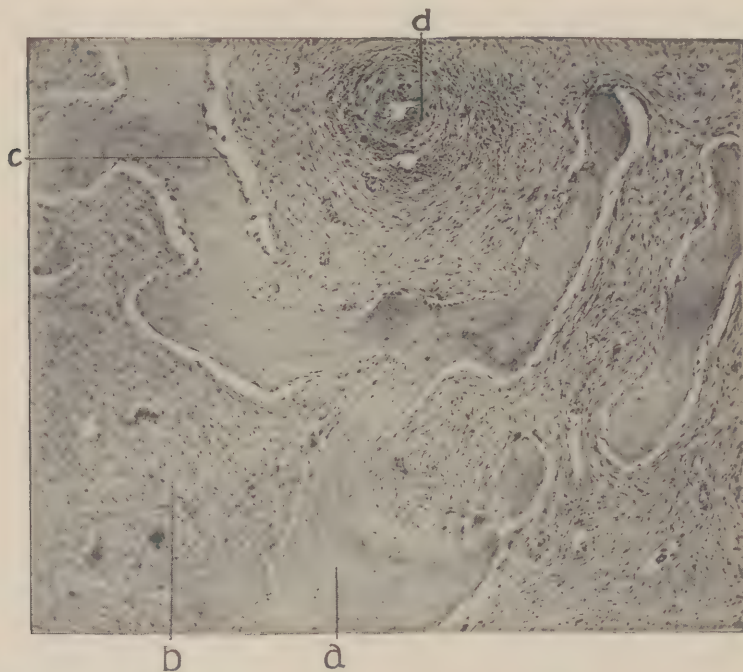
FIG. 424.—Microscopic section of a lesion of osteitis fibrosa cystica, showing bony trabeculae
with fibro-connective tissue lying between them. (*Meyerding.*)

which may be curetted away. Healed fractures with angular deformity, may
also be treated by the usual corrective measures, supplemented by removal of the
diseased bone in the neighborhood. Fractures that will not unite because of the
diseased condition of the ends of the affected bone, may be excised, and rein-
forced by transplantation. The cysts and giant cell tumors may be removed by
the curet, after which they do not, as a rule reappear. The benefit to be
obtained by these measures, will, however, depend upon the circumscription or
diffusion of the lesions, and the extent of bony invasion and destruction at the
time the patient seeks advice. The periosteum can usually be counted upon to
react normally in assisting the repair, as it usually escapes disease and
destruction.

It was necessary to say so much about the presence of cysts in describing the
changes in osteitis fibrosa cystica and the related disturbances, that the reader
may have been left in some doubt lest the presence of a cyst may not be indica-
tive of that disease. To remind him that that is not the case, and to recall the
various other cysts occasionally to be found in the bones, the following tabu-

FIG. 425.—Osteitis fibrosa cystica, with fracture of the right radius.   The cyst is limited to the diaphysis of the bone.   (*Meyerding.*)

FIG. 426.—Cystic degeneration—osteitis fibrosa cystica (?)—of the bones of the hand, especially affecting the metacarpal and phalanges of the little finger and the phalanges of the fourth.   The contents of the cysts were found at operation to be jelly-like.   (*Meyerding.*)

lation is introduced. Upon looking it over it will be discovered that all of the cysts tabulated have already received mention elsewhere, so that further separate mention of them is unnecessary.

BONE CYSTS

I. Affecting the maxillary bones only:
Arising through malformation of the teeth:
    1. Cystic adamantinoma.
    2. Dentigerous cysts.
II. Affecting the long bones chiefly:
Arising through the colliquation of solid tissue:
    1. Cysts at or near the epiphyses resulting from colliquation of remnants of the embryonal cartilage.
    2. Cysts in morbid growths:
    (a) Sarcoma of various types.
    (b) Benign giant cell tumors.
        Hemorrhagic (chocolate) cysts.
        Serous cysts.
    (c) Chondromas.
    (d) Secondary carcinomas.
III. Affecting any or many of the bones:
  A. Resulting from local disturbances.
    1. Cysts following the absorption of the contents of abscesses.
    2. Cysts following the absorption of the blood in hemorrhages.
  B. Resulting from generalized disturbance.
    Osteitis fibrosa cystica. ⎰ Fibrous cysts.
    Osteitis deformans.   ⎱ Giant cell tumor cysts.
    Osteomalacia
  C. Resulting from infestation by parasites.
    Echinococcus or hydatid cysts.
  D. Dermoids.

DISEASES OF THE JOINTS

ARTHRITIS

Arthritis, in its most simple form, not infrequently results from external traumatism without infection. With this single exception, all the varieties and all of the cases, whose causes are known, are found to be infectious, and by inference based upon resemblance, those whose causes have not been determined are supposed to be. Few cases are primary—that is dependent upon the admission of micro-organisms to the joint through external traumatic injury:— the great majority are secondary, and depend upon micro-organisms brought to the joint by the circulating blood. Arthritis, therefore, most frequently makes its appearance as a complication or sequel of some infectious disease in which bacteria are known to circulate in the blood, either as the primary and essential cause, as in typhoid fever, or as secondary invaders, as in scarlatina.

Of the infectious diseases in which arthritis has been observed to occur either as a complication or sequel, the list is long and includes, pyemia, septicema, endocarditis, pueperal fever, scarlatina, gonorrhoea—including the vulvovaginitis of little girls and the gonorrhoeal ophthalmia of infants,—pneumonia,

measles, typhoid fever, typhus fever, small-pox, whooping cough, influenza, pneumonia, diphtheria, dysentery, mumps, glanders, erysipelas, and tonsillitis. The relation of the tonsils to disease of the joints, especially that variety popularly designated "rheumatism," has of late years attracted wide-spread attention. There can be no doubt that the tonsillar crypts commonly harbor micro-organisms, among which both the Streptococcus viridans and Streptococcus hemolyticus are common. As in all cases of tonsillitis there is a substantial increase in the number of these organisms, and the dilated condition of the lymphatics makes certain that some of them descend through the cervical lymphatics to finally enter the circulation, apprehension concerning the safety of the joints is aroused in all cases of tonsillar disease, and it is almost universally recommended that the organs be carefully treated and if necessary removed. It is not impossible that micro-organisms may frequently—even continuously—enter the circulation through seemingly normal tonsils, and that thus arise cases of endocardial, joint, and other deeply seated diseases for the occurrence of which the term "idiopathic" was formerly employed. What is true of the tonsils may be partly true of other parts of the body. Thus, a patient with pyorrhoea alveolaris, chronic urethritis, appendicitis, cholecystitis, or diverticulitis of the colon, may be in danger of having his joints receive micro-organisms from the circulation, into which they have accidentally entered.

Arthritis caused by external trauma is limited to the injured joint—is *monoarticular*—arthritis caused by micro-organisms disseminated through the blood commonly affects several joints; is *polyarticular*.

The damage affected must be in proportion to the number and virulence of the micro-organisms, to the healthy or damaged state of the joint tissues, and to the resisting power of the individual. On this account the actual results differ in different cases through mild and ephemeral irritation, exudative accumulation, to purulent destruction, and later fatal systemic infection from the diseased joint.

Some joints becomes infected through the perforation of osteo-myelitic abscesses. It would seem as though this serious complication might be avoided if X-ray examinations of the bone and joint were made early enough to locate the actual seat of the disease.

I. *Serous Arthritis*.—This is also called simple arthritis, non-suppurative arthritis, and acute synovitis. It is almost always mono-articular, and is usually traumatic and non-infectious. It is characterized by serous effusion i.e., considerable increase in the quantity of synovial fluid. Opportunity to examine the interior of such joints is rare, but from what has been observed, supplemented by analogy with other inflammatory disturbances of similar character, it seems as though the trouble begins with hyperemia of the synovial membrane, and excessive secretion of fluid until the joint is distended, and its tissue edematous. The joint becomes weakened, its ligaments relaxed, and it is kept flexed. There may be pain and heat. It requires about three days for the exudation of the fluid to reach its maximum, but may require weeks for its later absorption. Ordinarily, however, perfect recovery ensues. But if the joint is not kept at rest, the absorption of the fluid is retarded, and if the patient's occupation or activity

lead to additional trauma, the condition may become chronic, the joint permanently weakened and more or less displaced. Such joints may be regarded as in a condition of diminished resistence, and in them any micro-organisms received from the blood may provoke more destructive disease.

II. *Sero-fibrinous Arthritis.*—This is commonly known as *rheumatism.* It is also called *polyarthritis rheumatica,* acute articular rheumatism, and acute rheumatic fever, because of associated general febrile reaction. It is undoubtedly infectious, micro-organisms, chiefly streptococci being occasionally cultivable

FIG. 427.—Posterior view of a normal ankle-joint injected with gelatine, to show the numerous small protrusions of synovial membrane through the posterior ligament. (*From a specimen in the museum of St. Thomas's Hospital; pictured by Bowlby and Andrewes.*)

from the joints, and sometimes from the blood of the patients. Several or many joints may be involved simultaneously or successively. There is considerable, and sometimes very severe pain. The joints redden, and swell, as an exudation consisting of serum with flakes of fibrin accumulates and distends them. They never suppurate.

The duration varies, and recovery is complicated and retarded by the presence of the fibrin which cannot immediately be absorbed, but adheres to the articular cartilages and synovial membranes, whose surfaces beneath the adhesions become denuded of the endothelium, and may granulate with the formation of fibrous adhesions by which subsequent mobility is diminished— *partial ankylosis.* Later manipulation and continued use may diminish these, so that the condition usually improves as time goes on. The majority of cases recover completely.

III. *Purulent Arthritis.*—In these cases the inflammation is suppurative and destructive, descending to the deeper structures of the joint, especially to the cartilages.

The condition may be primary, i.e., result from direct traumatic infection of the joint, as from gun-shot wounds, surgical operations etc. Or, it may be secondary to osteo-myelitis, abscesses of the bone opening into the joint; or, it may be engrafted upon a simple serous arthritis, either through carelessness

in aspirating the joint, bacteria being introduced during the operation; or, brought to the joint by the blood. Or, it may result from the admission to the normal joint of bacteria brought by the blood.

From the synovial membranes which are deeply congested, the usual serous fluid escapes, but with it also escape the multitudes of leucocytes that transform it to pus. There is great pain, redness and swelling, and the patient usually suffers considerable fever. The disturbance may end at this stage, and recovery begin, but unless the joint is opened, and the pus evacuated, the inflammation usually penetrates more deeply, and the synovial membranes
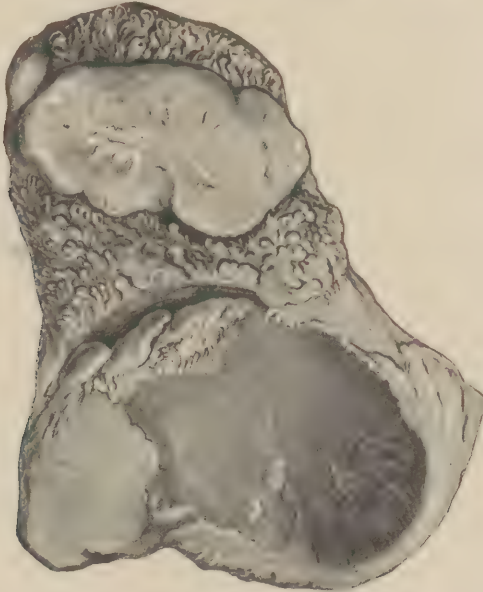
Fig. 428.—The patella and articular surface of the tibia from a case of osteo-arthritis. The edges of the articular surface are deformed by ecchondrosis, and the synovial membrane is covered with hypertrophied synovial fringes. (*Bowlby and Andrewes.*)

swell, become penetrated by newly formed blood vessels, develop what is commonly spoken of as "*pannus*," that is to say, granulation tissue, attach themselves to the cartilages, and effect destruction changes in them.

As cartilage has no blood vessels of its own, but is nourished by its perichondrium, a joint opened at this stage, and having the purulent accumulation washed out, will show apparently normal bluish white cartilage, to which the synovial membranes are adhering here and there. If such an adhesion be broken, and the subjacent cartilage exposed, it will be found to be eroded, and its surface reddened, fibrillated and softened. Such erosion may continue until all of the cartilaginous tissue disappears, though rarely does the condition progress to such a point. The ligaments and other structures entering into the composition of the joint, and the tissues immediately adjacent to it may also be more or less infiltrated with the pus, and thereby softened and destroyed, so that the bones are no longer held in position, but partly dislocated. The limb is always flexed. With such extensive pyogenic infection it is easy for the micro-organisms

to enter the lymphatics or the blood stream, so that not a few patients succumb to generalized infection. If, however, the joint be opened and thoroughly cleansed and drained, recovery may at any time begin. The condition following recovery, however, will always be far from normal. Cartilage having scarcely any power of regeneration, heals through the formation of fibrillar connective

FIG. 429.—Arthritis deformans (degenerative form). Erosion of head of femur with disloca-
tion to a new flattened joint surface on the ilium. (*MacCallum.*)

tissue which binds the denuded bones together —*false ankylosis*—or, if the destruction of the cartilage be more complete, the ends of the bones, may be connecting by a bony bridge, and immovably fixed—*true ankylosis*.

In neglected cases the pus may penetrate into the spongy tissue of the articular end of one of the bones and cause complicating osteitis, which, in turn, may go on to osteomyelitis.

The particular micro-organism engaged in the inflammatory process can sometimes be cultivated from the lesions, but they are apt to be sterile.

Some variations in the clinical picture, the pathological changes and the final outcome have to do with the particular micro-organisms engaged. Thus, the streptococci from the throat that excite rheumatic polyarthritis commonly

simultaneously affect a number of joints causing mild sero-fibrinous disease; gonococci usually affect but one joint, most frequently the knee, ankle or wrist. Of 755 cases of gonorrhoeal arthritis examined by Northrup, more than half had this distribution. Moreover, of the purulent forms of arthritis, that caused by the gonococcus is the least destructive, the greater number of the cases ultimately recovering without substantial deformity. Pneumococcic arthritis seems to be particularly dangerous. Cave examined the histories of 31 cases and found that 23 of them eventually died. Typhoidal arthritis if localized in a single joint is apt to be very destructive, but if distributed over a number
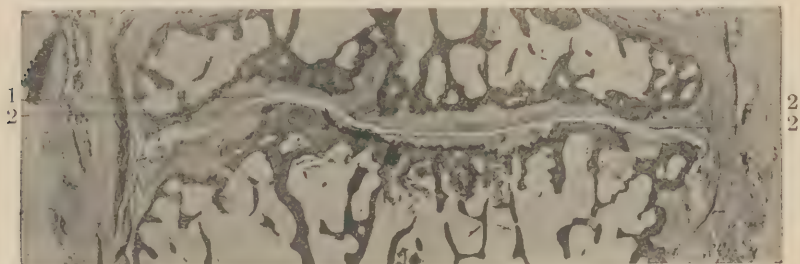
Fig. 430.—Degenerative arthritis deformans. Phalangeal joint, showing irregular joint surface, (1) with exposed eburnated bone (2, 2). (*Nichols and Richardson.*)

seems of be less severe and less destructive. Influenzal arthritis is usually in itself, not severe or destructive, but seems to initiate subsequent changes resembling those of arthritis deformans. These differences, however, cannot be depended upon in making the prognosis, as it is not always the essential microorganisms of the disease that do the damage, but as frequently the associated secondary invaders. Thus, in scarlatina, it is not the unknown, or doubtfully known micro-organism of that disease that brings about the arthritis, but the streptococci: the same is true of variola.

IV. *Arthritis Deformans.*—This affection also called *rheumatoid arthritis*, is essentially chronic from the beginning, and has nothing to do with any of the affections previously described. Instead of beginning with a serous, sero-fibrinous or purulent exudate there is gradual destruction of the articular cartilages and bony tissue below, with irregular new formation of bone about the articulations, and final partial or complete ankylosis. As no two authorities seem able to come to an entire agreement as to the cause, the sequence of events, or the characteristic lesions of this disease, it is difficult to describe it. Some believe it to be infectious, some think it metabolic and nutritional, and some even suspected that it is of endocrinal origin. It undoubtedly assumes different appearances in different joints and in different stages, if not in different people.

It can scarcely be said to be a surgical affection, any more than a medical one, as it is not amenable to operative treatment. But before describing its lesions, it is necessary to call attention to several related, if not identical conditions.

The first is *Sill's disease*, which occurs in childhood, usually before the second dentition, and is frequently, if not usually, mistaken for acute articular rheumatism, because of its tendency to affect several joints simultaneously. It may

entirely recover, or it may become chronic and result in thickening of the joint and the formation of bony and cartilaginous overgrowths like those of the arthritis deformans of adults. It is doubtful whether these acute and chronic forms are identical.

The second, is *malum coxae senilis*, or senile disease of the hip joint. This affects but one joint usually the hip, rarely the knee, thus differing from arthritis deformans in distribution, though effecting seemingly identical changes.

Fig. 431.—Typical deformity of the hands in arthritis deformans. The patient, rendered helpless, was long an inmate of the Philadelphia General Hospital.

Among the cases generally regarded as arthritis deformans there are, however, probably included several different conditions of different etiology, the similarity of whose lesions require them to be considered together.

Arthritis deformans is most frequent in women. It begins in middle life and progresses for many years, simultaneously affecting many of the smaller joints, especially those of the phalanges of the hands and feet, though it may affect those of the wrists, ankles, vertebral column, or temporo-maxillary articulations.

The disturbance seems to begin in the synovial fringes, and may be dry, or begin with more or less sero-fibrinous exudation. The joint cavity becomes distended and there is some pain. The fingers may become fusiform, or individual joints may enlarge, or nodes may form about the joints. Granulation tissue—pannus—soon appears at the margins of the synovial fringes, which enlarge through the formation of papilliform outgrowths that sometimes assume considerable size, chondrify or even ossify, and may pinched off so as to become free bodies—*joint mice* and *rice bodies*—moving about in the joint cavity, occasionally becoming caught between the cartilages, locking the joint, and irritating it so as to add acute synovitis to the already existing disturbance. The pannus soon effects cartilaginous erosion followed by fibrous union, and false

ankylosis increasing from the periphery toward the center of the joint. At the same time that the joint is thus made immobile, the edges of the articular cartilages overgrow with the development of ecchondroses, and the adjacent periosteum being stimulated adds new bone to the joint margins—osteophytes— that not infrequently becomes eburnized. Softening, erosion, fibrillation, and disappearance of the cartilages leave the articular surfaces of the bone, in cases
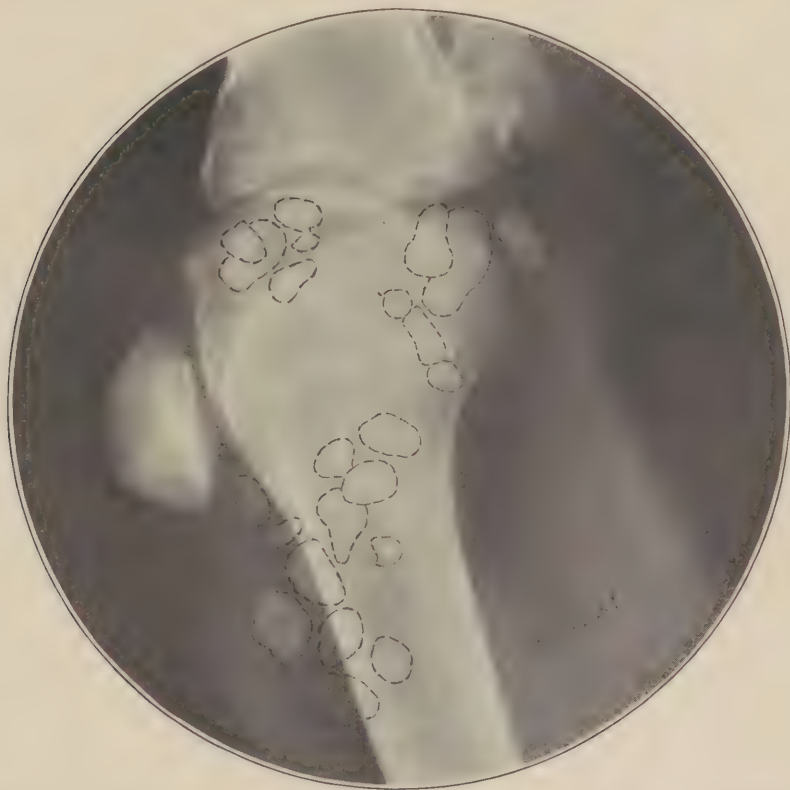
FIG. 432.—Multiple loose osteo-cartilaginous bodies in the knee-joint. (*Meyerding.*)

in which there is no ankylosis, to rub upon one another in such manner that they are worn into deep grooves and the surfaces polished. As there is no suppuration by which the osseous tissue is destroyed, and as new formation of cartilage seems to be impossible, the bone reacts by increasing in density and the uncovered articulating surfaces become eburnized, at the same time that the margins proliferate so as to form a considerable bony overhang. Hernial protrusion of the synovial membrane through weakened points in the capsular ligament may lead to the formation of *synovial cysts*, especially behind the knee joint.

Immobility of the joint from fibrous and osseous ankyloses, with fixation in an abnormal position determined rather by the cartilaginous destruction and new bone formation than by muscular action, is the final result of the disturbance. Thus the fingers are frequently directed toward the ulnar side of the

hand, the middle joints extended, and the terminal joints flexed, while the thumb is apt to be flexed at its first joint, and extended at the second.

The disease is usually slow, insidious and progressive, many years elapsing before a degree of deformity that renders the victim helpless is reached. But in some cases the disease having reached a certain point, seems to stop, and during subsequent years makes no further progress. In a few cases the extreme degree of deformity and fixation are reached in a few years.

Fig. 433.—Nineteen loose bodies removed from the anterior compartment of the joint shown in preceding illustration, by a median incision. (*Meyerding*.)

Gout

Gout is certainly not a surgical affection in the strict sense. It is a constitutional disturbance of metabolic nature, characterized by defective elimination of uric acid, salts of which being retained in the body, are deposited here and there, especially in the joints—*arthritis urica*. Why particular joints should thus suffer is a question difficult to answer, but is supposed to be primarily referable to the fact that the joints constituting the seats of election are frequently subject to mild traumatism by which they are predisposed to the deposits.

The affection is paroxysmal, that is, characterized by occasional, and sometimes periodic attacks. It begins with the deposition of salts of the urates in the substance of the articular cartilages of the joints, at which time there is swelling and great pain. After a varying period the acute symptoms wane, and the patient enters upon an interval, during which there is always some pain and disability.

If the joint be examined during the interval, the deposits of uratic salts will be shown by dirty white or greenish opacity of the cartilages, a microscopical section of which enables one to discover them in the form of a cicular crystals deposited between the fibrillating substance that wears away at the surfaces of contact, leaving erosions or ulcerations. If the lesion examined be old, and

much cartilage destroyed, the uratic deposits may be found to have extended into the adjacent osseous tissue.

During an attack or paroxysm of the disease, one sees in addition, the signs of acute arthritis—congestion of the synovial fringes, effusion of fluid into the joint, edema of the ligaments, and added ulcerations of the articulating surfaces. In the course of time, and following upon numerous attacks, the joint cavity becomes more or less filled with a mushy amorphus material rich in urates. Occasionally some of this is expressed between the loosened tissue of the capsular

FIG. 434.—Gout. Uratic tophi about the finger-joints. (*MacCallum*.)

ligament and appears as nodes beneath the skin, which may later atrophy and expose chalky masses—*joint tophi*. More rarely similar uratic deposits in the connective tissue of the subcutaneous fascia, or elsewhere in the fascia, occur in association with, or independently of joint disease, as *tophi*. A common seat of these is the subcutaneous tissue of the external ear.

The most characteristic gouty lesion occurs at the metatarso-phalangeal joint of the great toe, and constitutes *podagra*. A similar disturbance of the finger joints is known as *chiragra*, or of the knee joint as *gonagra*.

In any case painful considerable enlargement of the joint with varying deformity results.

TUBERCULOSIS OF THE JOINTS

It is not impossible that tuberculous disease of a joint may arise, through the lodgment, in one of the tissues of the joint, of bacilli brought by the blood from

the alimentary canal or from the lung into which they have been ingested or inspired. In such cases the disease of the joint is *primary*. Probably, however, the infection more frequently results from the distribution through the blood of bacilli from diseased lungs or lymph-nodes and is *secondary*. But the greatest number of tuberculous joint cases arise in an entirely different manner, namely through the extension of the disease to the adjacent joint from a tuberculous bone.

The disease is most frequent in childhood, and the joints most frequently affected are the hip and the knee. Future more frequent and careful X-ray examination of the bones in the cases of "growing pains" may reveal the small diseased foci in the bones early enough to enable their proper treatment to prevent the extension of the disease to the joints.

In the primary cases, the first tissue to be affected seems, in most cases, to be the synovial membrane. In cases infected by extension from the bones, the bacilli reaching the joint are distributed over the surface of the synovial membrane, the result in either case being the appearance in the tissue of the synovial membrane, of typical miliary tubercles. As they grow, the membrane becomes congested, and a granulation tissue pannus appears at its border, which becomes adherent to the cartilages and ligaments.

The granulation tissue soon erodes the cartilage as in arthritis, making it appear porous, or like the top of a pepper-box, dotted with small defects.

All about its margins the granulation tissue proceeds to undermine the cartilage, detaching it from the bone of the articulating surfaces, and permitting infection of the subjacent cancellous bony structure. In those cases that originate in the bone, the morbid process penetrates the cartilage, or burrows between it and the bone to its margin, when it finds its way into the joint cavity. Thus the cartilages may be undermined and partly or even completely detached from the bone before the invasion of the more superficial tissues of the joint takes place and it may be difficult or impossible to determine how the invasion of the joint first began. The tuberculous granulation tissue continually increases—fungous tuberculosis -eroding and destroying the cartilages which fibrillate, soften and gelatinize, filling the joint cavity with gelatinous viscid fluid, to which is soon added the products of its caseation. All cases do not show an equal amount of caseous change, some remaining productive rather than degenerative, and presenting an appearance that can only be recognized as tuberculosis through a microscopic examination of sections of the tissue.

The infectious process gradually involves the ligaments and tendons, and gradually works its way towards the exterior, sooner or later arriving at the skin surface, where it may appear in the form of soft gelatinous white material—*white swelling*—or melt away in the form of pus, which evacuates.

With the destruction of the cartilage, the cancellous tissue of the subjacent bone becomes involved, and undergoes tuberculous caries, crumbling away, and adding sandy material to the purulent and caseous joint contents.

While this destruction is in progress, the periosteum may form some new bone at the periphery of the diseased area, so that it becomes surrounded by irregular bony projections, some of which are extremely dense.

The progress of the disease is extremely slow, but the amount of destruction is sometimes extreme. At the hip joint—*coxalgia*—it may result in complete carious destruction of the head of the bone, dislocation, detachment of the great trochanter, softening of the ligaments, erosion and exfoliation of the cartilaginous rim of the acetabulum, destruction of the bony acetabulum, invasion of the iliac bone, and the formation of a large abscess behind the peritoneum on the inner side of the pelvis, at the same time that numerous fistulas are formed through the skin.

Generalized infection, is rare. Greater danger results from the prolonged suppuration, which may cause amyloid disease and death.

Fortunately, however, the disease is now rarely so severe, and when promptly and efficiently treated, may recover, leaving deformity corresponding with the extent of the destruction effected. The activity of the disease may cease at any stage, and recovery begin. It is then that the surgeon finds it best to intervene to facilitate healing by the removal of the caseous and necrotic accumulations, and transform the lesion, as nearly as possible into a clean wound. As the destroyed tissues can be but partly regenerated, healing must take place chiefly through the new formation of fibrillar connective tissue that replaces the lost parts, binds all together, and gives the limb rigidity through fibrous and bony ankylosis.

In complete bony ankylosis, the united bones may form a single structure, even, in some cases, having a common marrow cavity.

But recovery is not infrequently complicated by occasional foci of disease, in which living, tubercle bacilli become encapsulated or included in the newly formed connective tissue. Upon future occasions, should the resistence of the part be diminished through traumatic injury, or the general vital resisting power diminished, they may start the disease afresh.

Syphilis of the Joints

The only lesion it seems worth while to consider under this heading is that known as *Charcot's joint*, the *tabetic arthropathy*. Whether it be a manifestation of the syphilis or of the nervous disease resulting from the syphilis is not decided, but it is a distinct entity, and extremely destructive.

It may affect several joints, but is usually limited to one, affecting or order of frequency, the knee, hip, shoulder, foot and elbow.

In general symptomatology and course the affection bears considerable resembalance to severe cases of osteo-arthritis, though unaccompanied by as much pain.

The lesions bear considerable resemblance to those of the chronic senile form of arthritis deformans, the malum coxa senile, or arthritis ulcerosa sicca, but are much more rapid in development. The cartilages gradually disappear, after which follows a remarkably rapid and destructive frictional wearing away of the bones, which soon lose the entire articulating extremities and appear as if ground with a stone or file. That these must be in an advanced state of disease or degeneration before the actual disturbance of the joint asserts itself, seems

probable from the fact that in some cases considerable sized fragments break off. These do not behave like ordinary sequestra, but sometimes remain to be completely enclosed in newly formed bone of which there is usually so great an excess, that the entire joint cavity may be surrounded by an osseous encasement, the bones dislocated, and the joint made useless.

FIG. 435.—Two views of the knee-joint of a case of Charcot's disease, showing the wearing away of the bones and displacement of the articular surfaces. One femoral condyle has been completely worn away. (*Bowlby and Andrewes.*)

The disease sometimes develops with remarkable rapidity, preceding the nervous condition with which it is associated, and may run an equally rapid and destructive course. As the disease (tabes) with which it is associated is incurable, there is no tendency for the joint disturbance to recover.

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